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Dong Jiang (78243)
703-305-1345
U.S. Patent and Trademark Office
Art Unit 1646
dong.jiang@uspto.gov
CM1-10D08
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POINT OF CONTACT:
PAUL SCHULWITZ
TECHNICAL INFO. SPECIALIST
CM1 6B06 TEL. (703) 305-1954

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Date Picked Up: 8/26
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Searcher Prep/Review: 10
Clerical: _____
Online time: 10

TYPE OF SEARCH:
NA Sequences: _____
AA Sequences: 1
Structures: _____
Bibliographic: _____
Litigation: _____
Full text: _____
Patent Family: _____
Other: _____

VENDOR/COST (where applic.)
STN: _____
DIALOG: _____
Questel/Orbit: _____
DRLink: _____
Lexis/Nexis: _____
Sequence Sys.: _____
WWW/Internet: _____
Other (specify): _____

=> fil reg; d que 17

FILE 'REGISTRY' ENTERED AT 12:40:22 ON 19 AUG 2002
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STRUCTURE FILE UPDATES: 16 AUG 2002 HIGHEST RN 444143-26-4
DICTIONARY FILE UPDATES: 16 AUG 2002 HIGHEST RN 444143-26-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

L7 1 SEA FILE=REGISTRY ABB=ON THRLAGLLSRSGGMVKS NFV VPTNVGSKAF/SQSFP

*Seq ID 2, family search
(conservative substitution allowed)*

=> d 17 rn cn sql kwic nte

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS

RN 352232-71-4 REGISTRY

CN L-Phenylalanine, L-threonyl-L-histidyl-L-arginyl-L-leucyl-L-alanylglycyl-L-leucyl-L-leucyl-L-seryl-L-arginyl-L-serylglycylglycyl-L-methionyl-L-valyl-L-lysyl-L-seryl-L-asparaginyl-L-phenylalanyl-L-valyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-lysyl-L-alanyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 26: PN: US6268474 SEQID: 2 unclaimed sequence

SQL 30

SEQ 1 THRLAGLLSR SGGMVKS NFV VPTNVGSKAF

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HITS AT: 1-30

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FILE 'CAPLUS' ENTERED AT 12:40:46 ON 19 AUG 2002
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FILE COVERS 1907 - 19 Aug 2002 VOL 137 ISS 8
FILE LAST UPDATED: 18 Aug 2002 (20020818/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

L7 1 SEA FILE=REGISTRY ABB=ON THRLAGLLSRSGGMVKS NFVVPTNVGSKAF/SQSFP

L8 1 SEA FILE=CAPLUS ABB=ON L7

=> d ibib ab hitrn l8

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:560084 CAPLUS

DOCUMENT NUMBER: 135:153114

TITLE: Preparation of peptide antagonists of CGRP-receptor superfamily

INVENTOR(S): Smith, Derek David; Saha, Shankar; Abel, Peter W.

PATENT ASSIGNEE(S): Creighton University, USA

SOURCE: U.S., 24 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6268474	B1	20010731	US 1998-70504	19980430
US 2002068814	A1	20020606	US 2001-813345	20010320

PRIORITY APPLN. INFO.: US 1998-70504 A3 19980430

OTHER SOURCE(S): MARPAT 135:153114

AB Peptides R1-X-Z [Z is a vasoactive peptide fragment of at least 15 amino acids from calcitonin gene-related peptide (CGRP); R1 is an org. group; X is CO, SO2 or (CR2R3)n, where R2 and R3 are independently H or an org. group and n is an integer 1-10] were prepd. as antagonists of CGRP. Amino terminal modification of the vasoactive peptides is done to improve their ability to bind to a member of the CGRP-receptor superfamily. Thus, N-.alpha.-benzyl-, N-.alpha.-benzoyl-, and dibenzyl-h-.alpha.- or h-.beta.-CGRP(1-37) were prepd. by the solid-phase method and data for radioligand binding and inhibition of relaxation are tabulated.

IT 352232-71-4

RL: PRP (Properties)

(unclaimed sequence; prepn. of peptide antagonists of CGRP-receptor superfamily)

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> fil reg; d stat que 119; fil capl; d que nos 125
FILE 'REGISTRY' ENTERED AT 12:50:02 ON 19 AUG 2002
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DICTIONARY FILE UPDATES: 16 AUG 2002 HIGHEST RN 444143-26-4

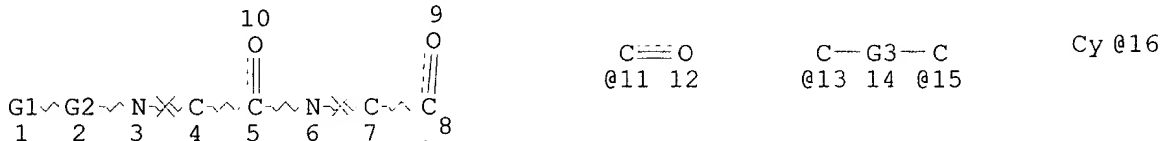
TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

L9 4834 SEA FILE=CAPLUS ABB=ON (CALCITONIN GENE RELATED PEPTIDE?)/OBI
OR CGRP/OBI
L10 226825 SEA FILE=CAPLUS ABB=ON ANTAGONI?
L11 1500218 SEA FILE=CAPLUS ABB=ON INHIBIT?
L13 486 SEA FILE=HCAPLUS ABB=ON L9(L) (L10 OR L11)
L14 SEL L13 1- RN : 4034 TERMS
L15 4034 SEA FILE=REGISTRY ABB=ON L14
L16 STR



Ak @17 Ak-F
@18 19

= Ring or chain bonds & nodes

Cy = any cyclic group
Ak = alkyl

VAR G1=16/17/18
VAR G2=11/SO2/C/13-1 15-3
REP G3=(0-8) C
NODE ATTRIBUTES:
NSPEC IS RC AT 4
NSPEC IS RC AT 7
CONNECT IS E1 RC AT 17
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 16
DEFAULT ECLEVEL IS LIMITED

G1 = R'

G2 = X

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
L19 332 SEA FILE=REGISTRY SUB=L15 SSS FUL L16

100.0% PROCESSED 1038 ITERATIONS
SEARCH TIME: 00.00.04

332 ANSWERS

FILE 'CAPLUS' ENTERED AT 12:50:03 ON 19 AUG 2002
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FILE COVERS 1907 - 19 Aug 2002 VOL 137 ISS 8
FILE LAST UPDATED: 18 Aug 2002 (20020818/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

L9 4834 SEA FILE=CAPLUS ABB=ON (CALCITONIN GENE RELATED PEPTIDE?)/OBI
OR CGRP/OBI
L10 226825 SEA FILE=CAPLUS ABB=ON ANTAGONI?
L11 1500218 SEA FILE=CAPLUS ABB=ON INHIBIT?
L12 486 SEA FILE=CAPLUS ABB=ON L9(L) (L10 OR L11)
L13 486 SEA FILE=HCAPLUS ABB=ON L9(L) (L10 OR L11)
L14 SEL L13 1- RN : 4034 TERMS
L15 4034 SEA FILE=REGISTRY ABB=ON L14
L16 STR
L19 332 SEA FILE=REGISTRY SUB=L15 SSS FUL L16
L20 57717 SEA FILE=CAPLUS ABB=ON L19
L22 11544 SEA FILE=CAPLUS ABB=ON L20(L) (THU OR BAC OR PAC OR PKT OR
DMA)/RL
L23 72 SEA FILE=CAPLUS ABB=ON L22 AND L12
L24 1055 SEA FILE=CAPLUS ABB=ON L9(L) RECEPTOR#
L25 48 SEA FILE=CAPLUS ABB=ON L24 AND L23

Roles THU - Therapeutic use
BAC - biological activity
PAC - pharmacologic ~~act~~ activity
PKT - pharmacokinetics
DMA - drug mechanism of action

=> d ibib abs hitstr l25 1-48; fil hom

L25 ANSWER 1 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:502819 CAPLUS
DOCUMENT NUMBER: 137:57577
TITLE: Irrigation solution and method for inhibition of pain
and inflammation
INVENTOR(S): Demopoulos, Gregory A.; Pierce, Pamela Anne; Herz,
Jeffrey M.
PATENT ASSIGNEE(S): Omeros Medical Systems, Inc., USA
SOURCE: U.S., 47 pp., Cont.-in-part of U.S. 6,261,279.
CODEN: USXXAM
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6413961	B1	20020702	US 1999-388837	19990901
WO 9619233	A2	19960627	WO 1995-US16028	19951212
WO 9619233	A3	19960919		
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RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 5820583	A	19981013	US 1996-670699	19960626
US 6261279	B1	20010717	US 1998-72913	19980504
PRIORITY APPLN. INFO.:			US 1994-353775	B2 19941212
			WO 1995-US16028	A2 19951212
			US 1996-670699	A1 19960626
			US 1998-72913	A2 19980504
			US 1998-98977P	P 19980902

AB A method and soln. for perioperatively inhibiting a variety of pain, inflammation, spasm and restenosis processes resulting from cardiovascular or general surgical, therapeutic and diagnostic procedures are described. The soln. preferably includes multiple pain and inflammation inhibitory agents, including at least one local anesthetic agent, and spasm inhibitory agents at dil. concn. in a physiol. carrier, such as saline or lactated Ringer's soln. Specific preferred embodiments of the soln. of the present invention for use in cardiovascular and general vascular procedures also include anti-restenosis agents. Several example formulations of irrigation solns. for arthroscopy, and for urol., vascular, cardiovascular and other procedures are provided. Also described are exptl. results from studies on the effect of histamine/serotonin receptor blockade on response to balloon dilatation of iliac arteries, studies on amitriptyline inhibition of 5-HT-induced knee joint plasma extravasation, and studies on the effects of a cardiovascular soln. on rotational atherectomy-induced vasospasm in arteries.

IT 342-10-9D, Kallidin, deriv. 71800-37-8
128270-60-0, Hirulog 138614-30-9, HOE 140
138680-92-9, [Des-Arg10]-HOE 140
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation solns. for inhibiting pain and inflammation at wound during surgical procedures)

RN 342-10-9 CAPLUS
CN Kallidin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

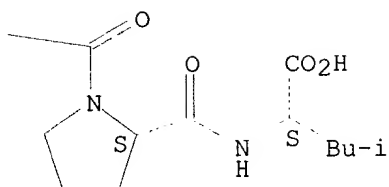
The chemical structure is a complex macrocycle containing several sulfur (S) and nitrogen (N) atoms. It features a central ring system with a sulfur atom at the top and a nitrogen atom at the bottom. The ring is substituted with various side chains: a long alkyl chain (CH₂)₃ with an amine group (NH₂), a long alkyl chain (CH₂)₄ with a carbonyl group (C=O), a hydroxyl group (OH), and a phenyl group (Ph). The structure also includes several amine groups (NH₂, NH) and amide groups (C=O, NH).

NC(=O)NCCCNC(=O)S[C@H](C(=O)N)C(=O)Nc1ccccc1

Absolute stereochemistry.

Chemical structure of compound 10, a complex macrocyclic molecule. It features a central ring system with multiple sulfur (S) and nitrogen (N) atoms. Substituents include a primary amine group (H_2N), a secondary amine group (NH), a hydroxyl group (HO), and a phenyl group (Ph). The structure is highly branched and contains several amide and thioether linkages.

PAGE 1-B

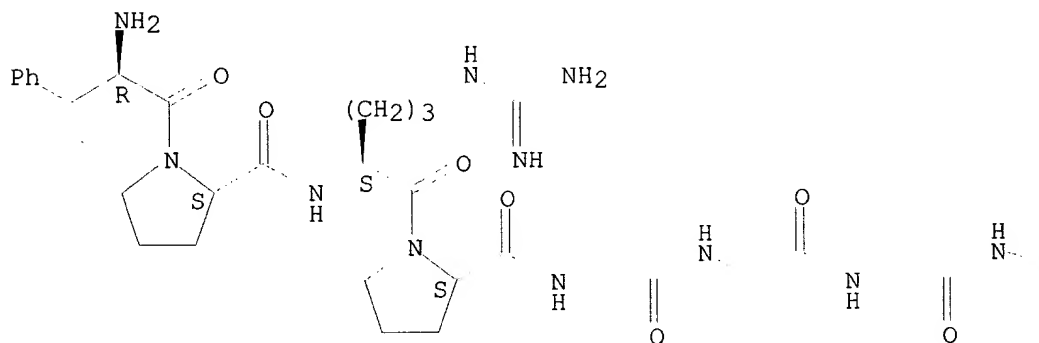


RN 128270-60-0 CAPLUS

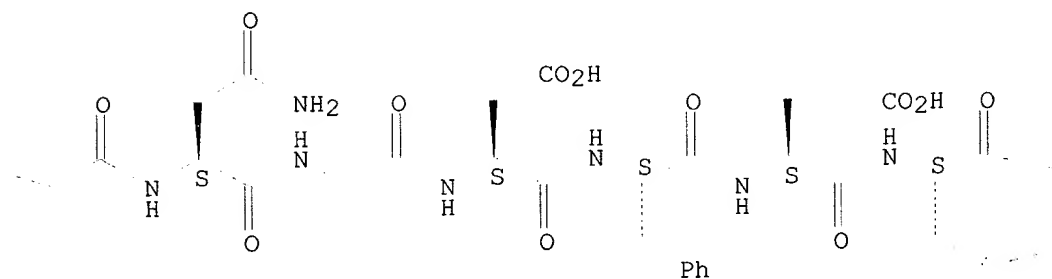
CN L-Leucine, D-phenylalanyl-L-prolyl-L-arginyl-L-prolyl-glycylglycylglycylglycyl-L-asparaginylglycyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-isoleucyl-L-prolyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

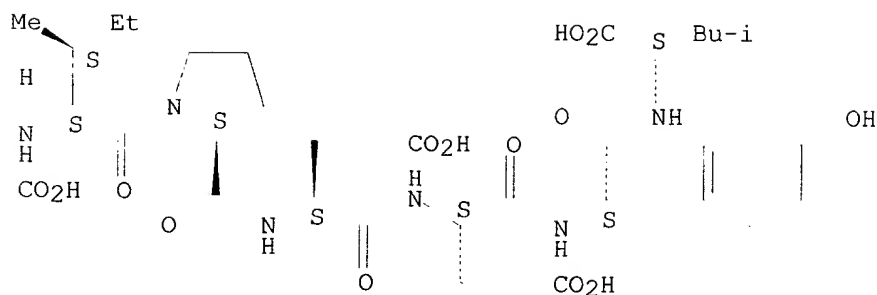
PAGE 1-A



PAGE 1-B



PAGE 1-C



RN 138614-30-9 CAPLUS
 CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl-, acetate (salt) (9CI) (CA INDEX NAME)

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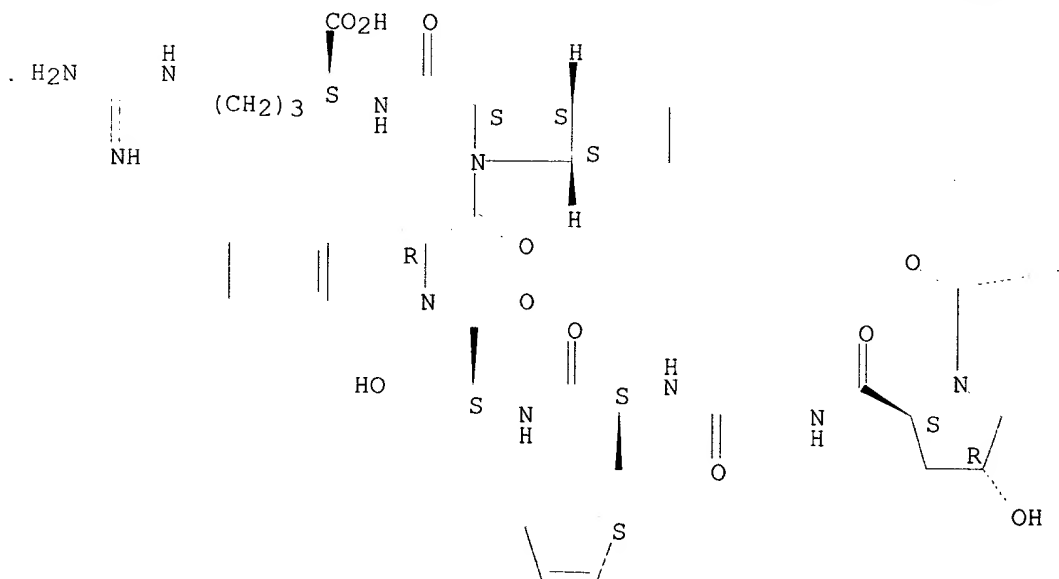
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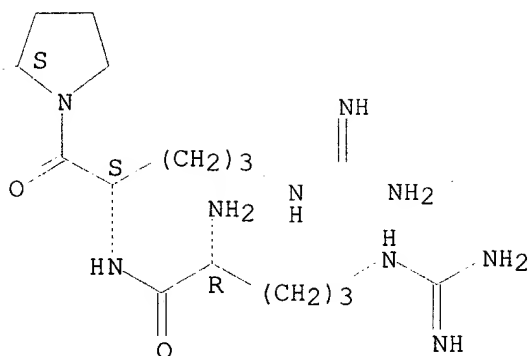
CDES *

Absolute stereochemistry.

PAGE 1-A



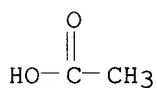
PAGE 1-B



CM 2

CRN 64-19-7

CMF C2 H4 O2

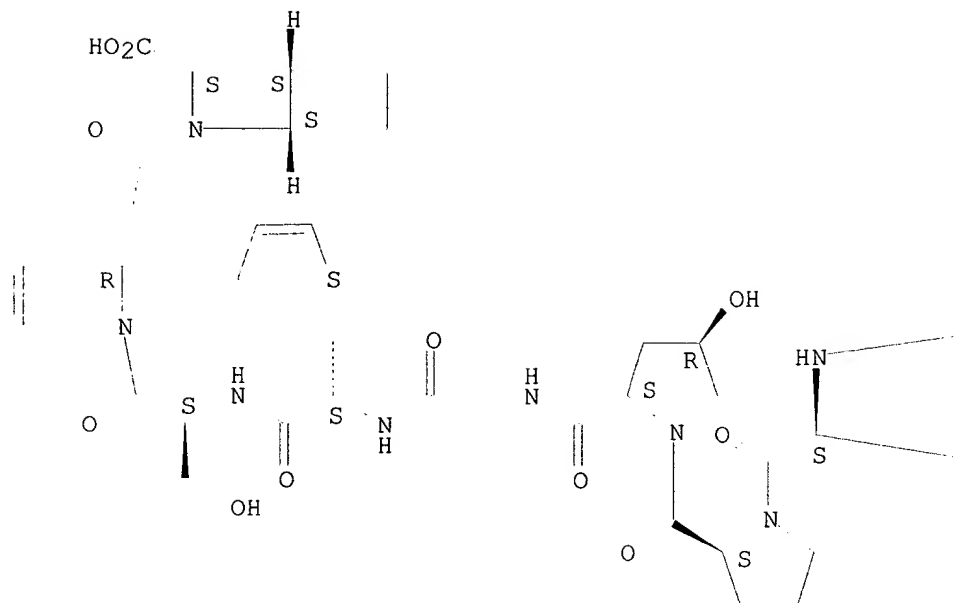


RN 138680-92-9 CAPLUS

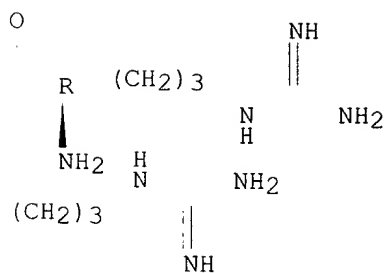
CN 1H-Indole-2-carboxylic acid, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyloctahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 92 THERE ARE 92 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:172487 CAPLUS

DOCUMENT NUMBER: 136:221745

TITLE: Irrigation solution and method for inhibition of pain and inflammation

INVENTOR(S): Demopulos, Gregory A.; Pierce-Palmer, Pamela; Herz, Jeffrey M.

PATENT ASSIGNEE(S): Omeros Medical Systems, USA

SOURCE: U.S. Pat. Appl. Publ., 58 pp., Cont.-in-part of Appl.

Searched by Barb O'Bryen, STIC 308-4291

No. PCT/US99/24625.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002028798	A1	20020307	US 2001-839633	20010420
WO 9619233	A2	19960627	WO 1995-US16028	19951212
WO 9619233	A3	19960919		
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US 6261279	B1	20010717	US 1998-72913	19980504
WO 2000023061	A2	20000427	WO 1999-US24557	19991020
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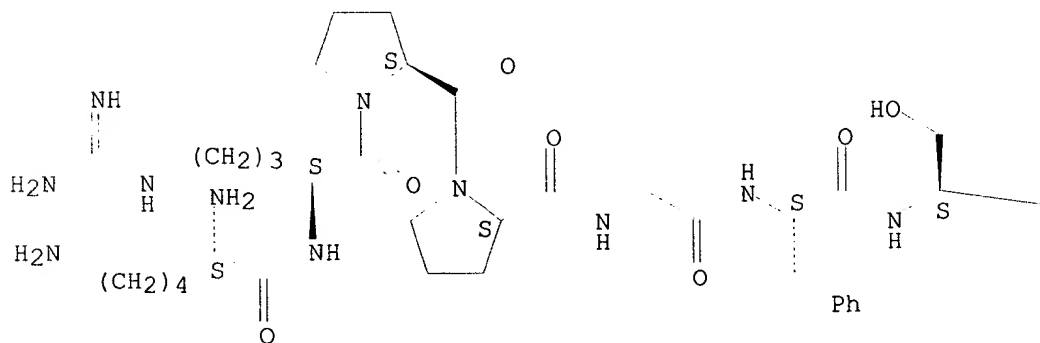
US 1994-353775 B2 19941212
WO 1995-US16028 A2 19951212
US 1996-670699 A2 19960626
US 1998-72913 A2 19980504
US 1998-105026P P 19981020
US 1998-105029P P 19981020
US 1998-105044P P 19981020
US 1998-105166P P 19981021
US 1998-107256P P 19981105
WO 1999-US24557 A2 19991020
WO 1999-US24558 A2 19991020
WO 1999-US24625 A2 19991020
WO 1999-US24672 A2 19991020
WO 1999-US26330 A2 19991105

AB A method and soln. for perioperatively inhibiting a variety of pain and inflammation processes at wounds from general surgical procedures including oral/dental procedures. The soln. preferably includes at least one pharmacol. agent selected from the group consisting of a mitogen-activated protein kinase (MAPK) inhibitor, an .alpha.2-receptor agonist, a neuronal nicotinic acetylcholine receptor agonist, a cyclooxygenase-2 (COX-2) inhibitor, a sol. receptor and mixts. thereof, and optionally addnl. multiple pain and inflammation inhibitory agents at dil. concn. in a physiol. carrier, such as saline or lactated Ringer's soln. The soln. is applied by continuous irrigation of a wound during a surgical procedure for preemptive inhibition of pain and while avoiding undesirable side effects assocd. with oral, i.m., s.c. or i.v. application of larger doses of the agents.

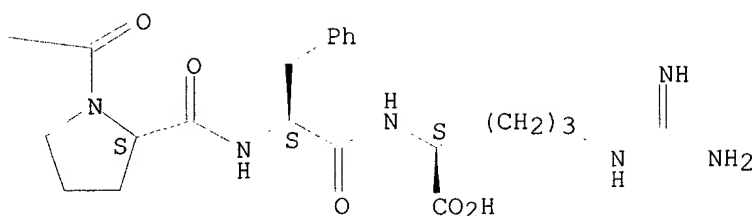
IT 342-10-9, Kallidin 128270-60-0, Hirulog
129623-01-4, GR82334 138614-30-9, Hoe 140
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation soln. for inhibition of pain and inflammation at wounds during surgical procedures)
RN 342-10-9 CAPLUS
CN Kallidin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

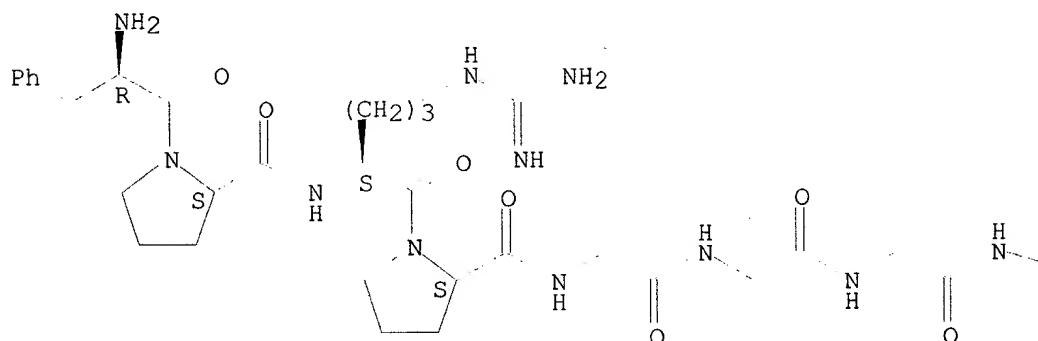


RN 128270-60-0 CAPLUS

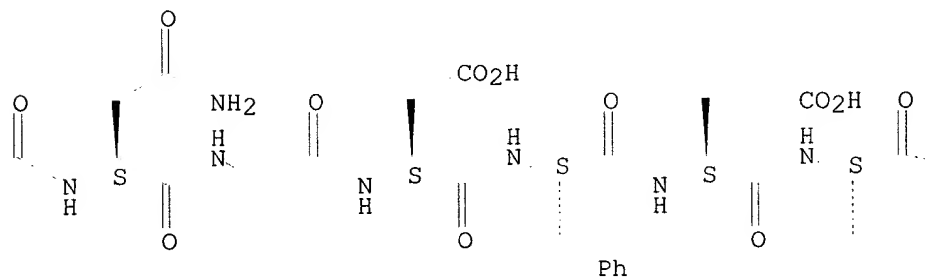
CN L-Leucine, D-phenylalanyl-L-prolyl-L-arginyl-L-prolylglycylglycylglycylglycyl-L-asparaginyglycyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-isoleucyl-L-prolyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

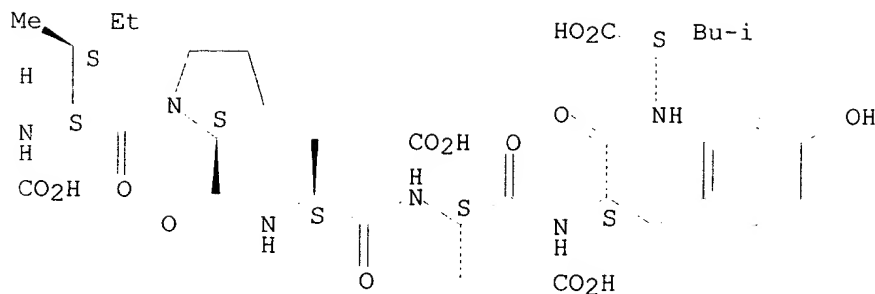
PAGE 1-A



PAGE 1-B



PAGE 1-C

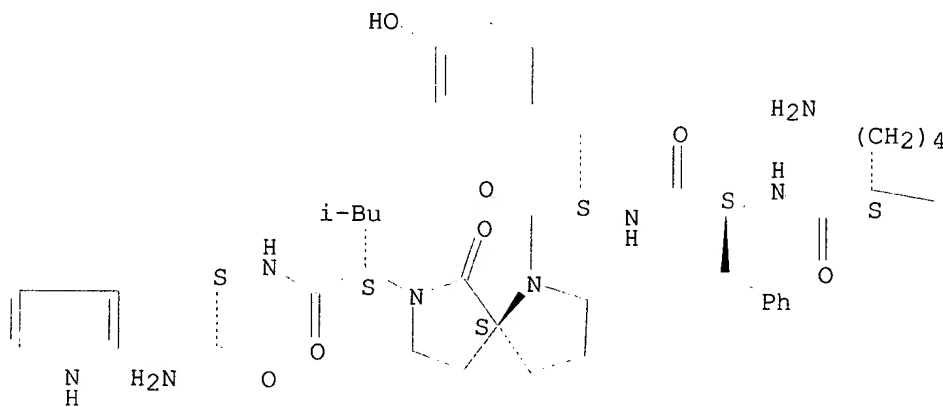


RN 129623-01-4 CAPLUS

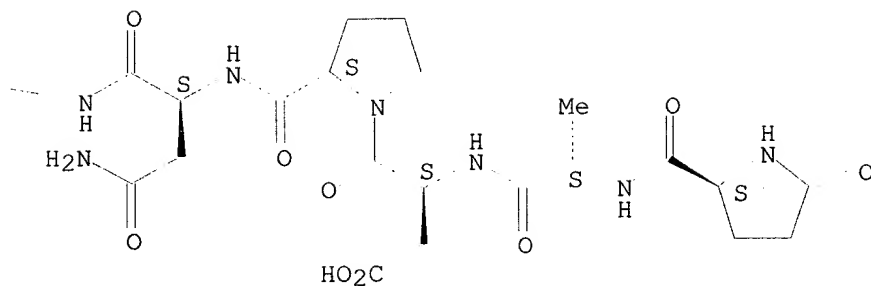
CN L-Tryptophanamide, 5-oxo-L-prolyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-lysyl-L-phenylalanyl-L-tyrosyl-(.alpha.S,5S)-.alpha.-(2-methylpropyl)-6-oxo-1,7-diazaspiro[4.4]nonane-7-acetyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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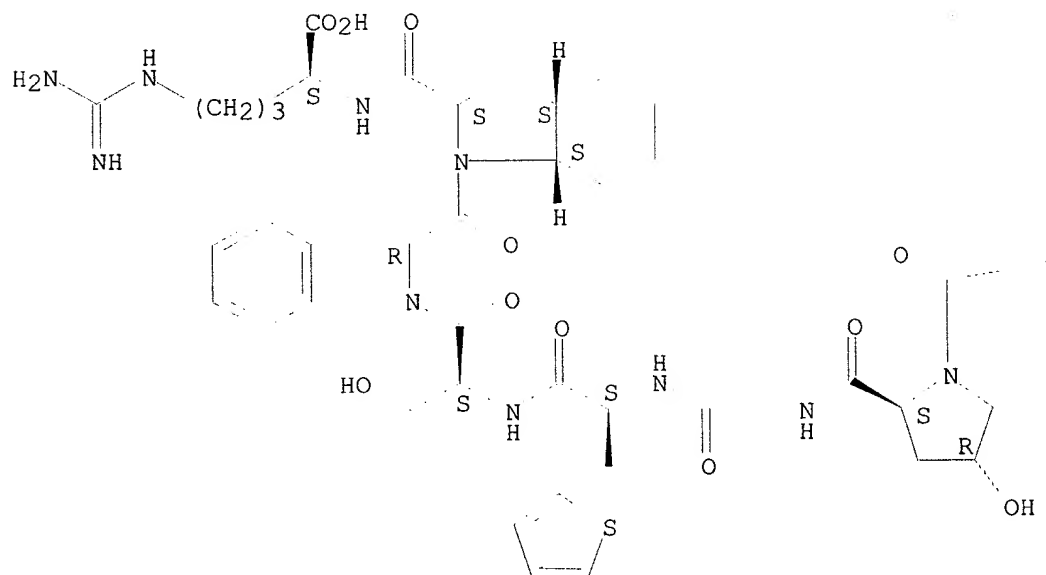
RN 138614-30-9 CAPLUS
 CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl-, acetate (salt) (9CI) (CA INDEX NAME)

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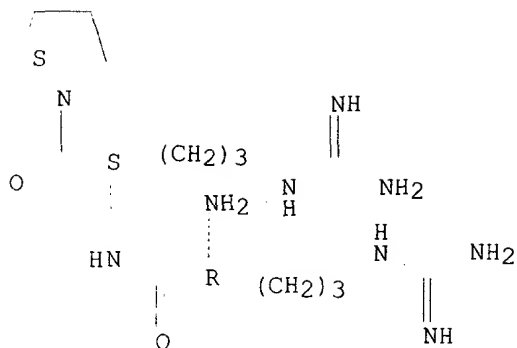
CRN 130308-48-4
 CMF C59 H89 N19 O13 S
 CDES *

Absolute stereochemistry.

PAGE 1-A

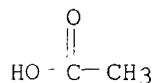


PAGE 1-B



CM 2

CRN 64-19-7
CMF C2 H4 O2



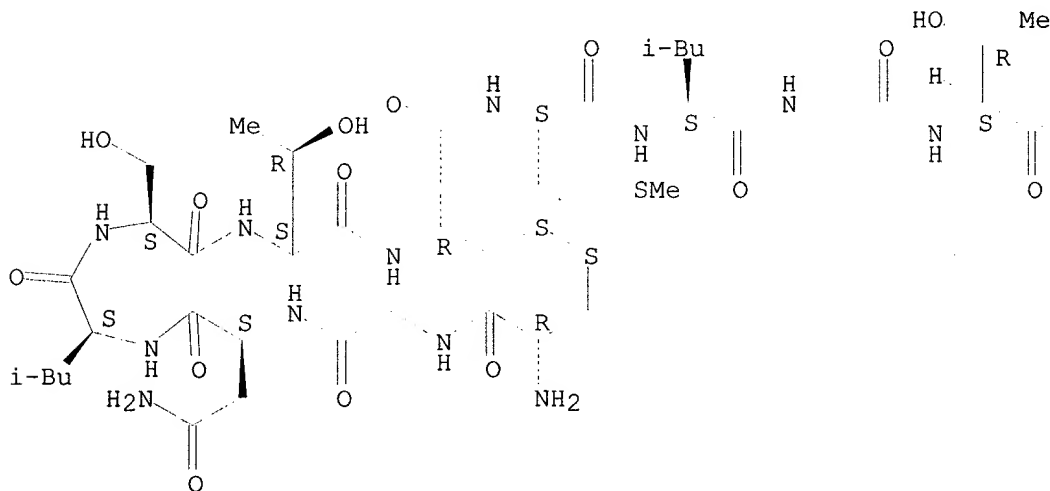
L25 ANSWER 3 OF 48 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:591784 CAPLUS
 DOCUMENT NUMBER: 135:353046
 TITLE: Effects of calcitonin, amylin, and calcitonin gene-related peptide on osteoclast development
 AUTHOR(S): Cornish, J.; Callon, K. E.; Bava, U.; Kamona, S. A.; Cooper, G. J. S.; Reid, I. R.
 CORPORATE SOURCE: Department of Medicine and School of Biological Sciences, University of Auckland, Auckland, N. Z.
 SOURCE: Bone (New York, NY, United States) (2001), 29(2), 162-168
 CODEN: BONEDL; ISSN: 8756-3282
 PUBLISHER: Elsevier Science Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Amylin and calcitonin gene-related peptide (CGRP) are homologous 37 amino acid peptides that are found in the circulation. Both peptides belong to the calcitonin family. Similar to calcitonin, amylin and CGRP inhibit osteoclast activity, although they are much less potent than calcitonin. Calcitonin is known to act on the latter stages of osteoclast development, inhibiting the fusion of committed preosteoclasts to form mature multinucleated cells; however, whether or not calcitonin acts earlier in the formation of the precursor osteoclasts is controversial. The question of osteoclast development has never been examd. with respect to amylin and CGRP. These issues are addressed in the present study. The authors studied the effects of calcitonin (salmon and rat), amylin (human and

rat), and CGRP (human and rat) in mouse bone marrow cultures stimulated to generate osteoclasts using 1.alpha.,25-dihydroxyvitamin D3. Calcitonin dose-dependently decreased the nos. of tartrate-resistant acid phosphatase (TRAP)-pos. multinucleated cells as well as TRAP-pos. mono-/binucleated cells at concns. >10⁻¹³ M. Amylin and CGRP showed similar effects at concns. >10⁻⁹ M. In addn., calcitonin substantially reduced the ratio of TRAP-pos. multinucleated to mono-binucleated cells, indicating an effect on fusion of osteoclast precursors. The present data establish that this family of peptides not only acts on mature osteoclasts but also inhibits their development in bone marrow cultures. This activity is shared by amylin and CGRP. The much greater potency of calcitonin than amylin and CGRP is consistent with the action of these peptides being mediated by calcitonin receptors.

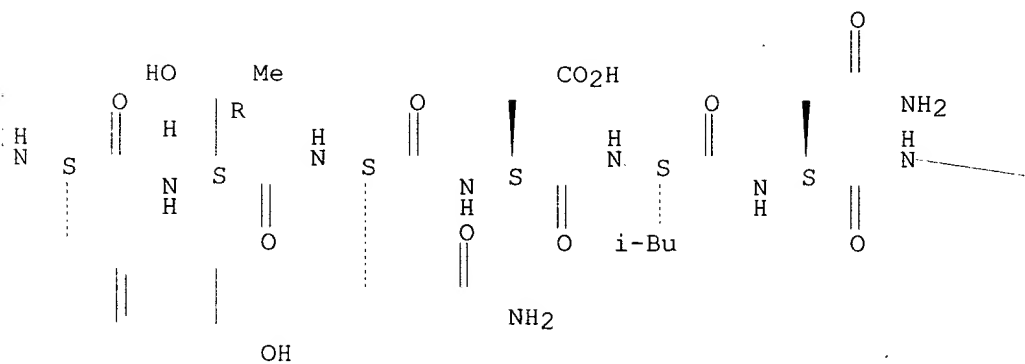
IT 11118-25-5, Rat calcitonin 47931-85-1, Salmon calcitonin
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); BIOL (Biological study)
 (calcitonin, amylin and calcitonin gene-related peptide effects on
 osteoclast development in mouse bone marrow cultures stimulated by
 1.alpha.,25-dihydroxyvitamin D3)
 RN 11118-25-5 CAPLUS
 CN Calcitonin (rat) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

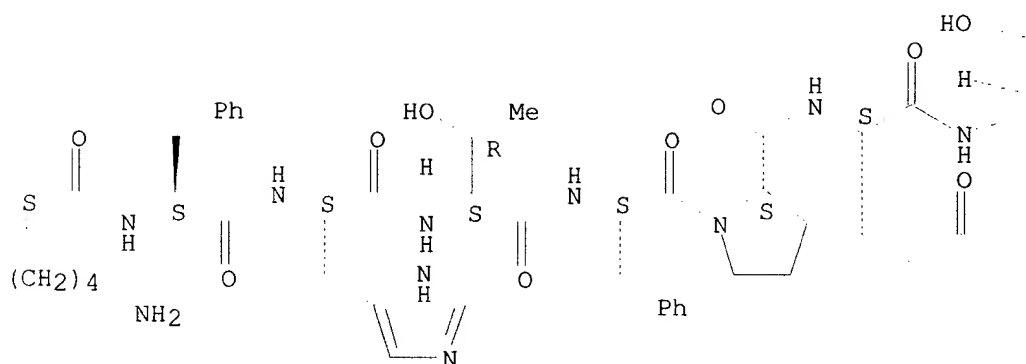
PAGE 1-A



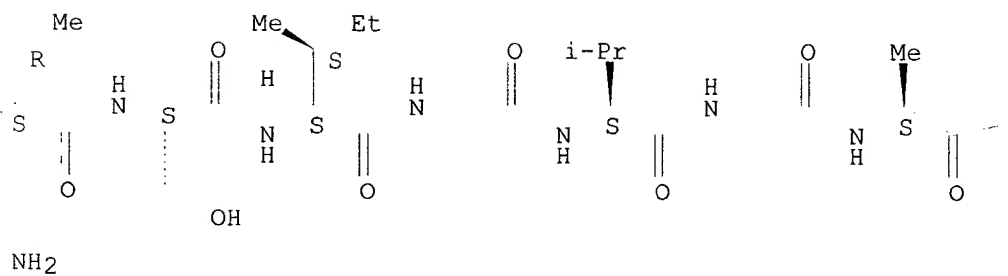
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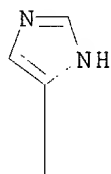
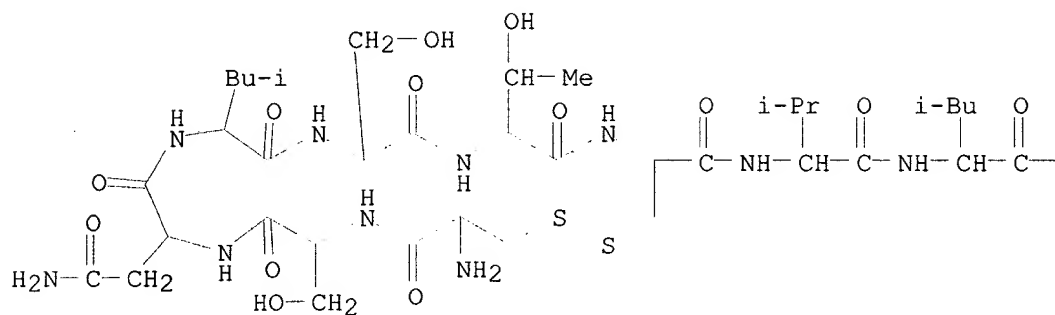


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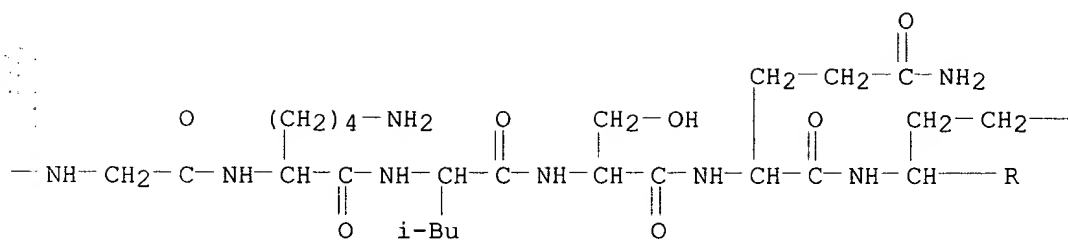


C[C@H](C(=O)[O-])N1CCSC1

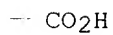
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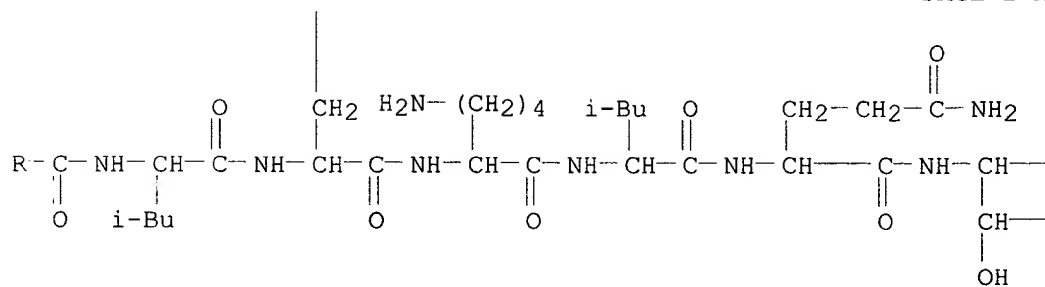
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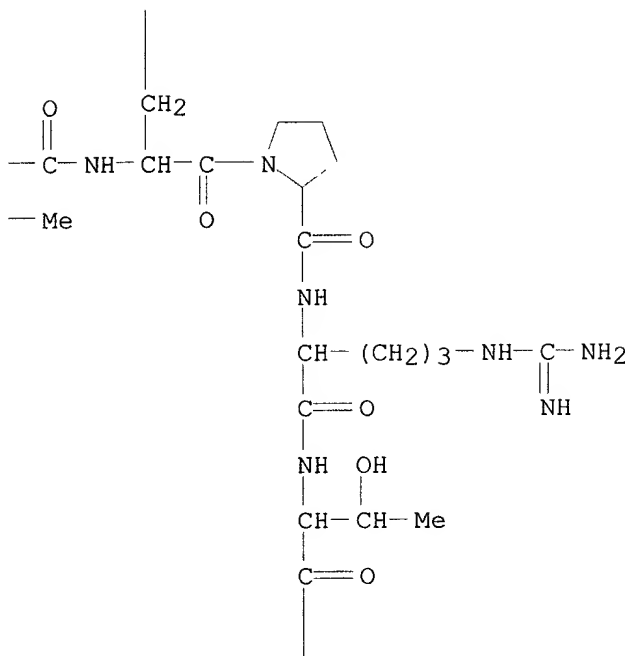
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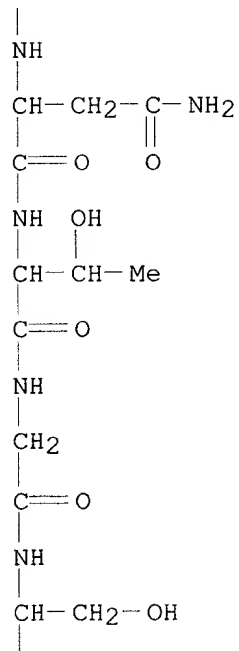
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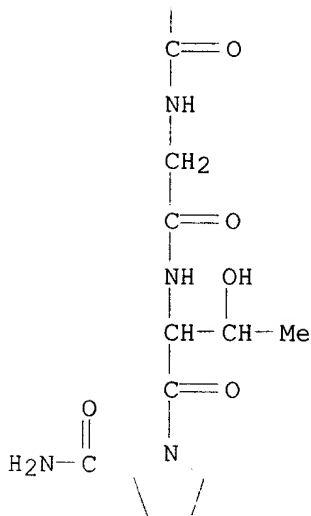
PAGE 2-B



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PAGE 4-B



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:575328 CAPLUS

DOCUMENT NUMBER: 136:67310

TITLE: Modulatory effect of two novel **CGRP**

receptor antagonists on nasal vasodilatory responses to exogenous **CGRP**, capsaicin, bradykinin and histamine in anesthetized pigs

AUTHOR(S): Malis, D.-D.; Rist, B.; Nicoucar, K.; Beck-Sickinger, A. G.; Morel, D. R.; Lacroix, J.-S.

CORPORATE SOURCE: Laboratory of Experimental Rhinology, Clinic of Otorhinolaryngology, University Hospital, Geneva, CH-1211, Switz.

SOURCE: Regulatory Peptides (2001), 101(1-3), 101-108

CODEN: REPPDY; ISSN: 0167-0115

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Calcitonin gene-related peptide (CGRP) is a 37-amino acid peptide and potent vasodilator agent located in sensory C fibers. Several functional studies suggest that CGRP could be involved in the vasodilatation of different vascular beds during neurogenic inflammation. We have studied, in pentobarbital anesthetized pigs, the antagonistic effect of local intra-arterial (i.a.) pretreatment with the analogs CGRP 8-37, [D31, P34, F35]CGRP 27-37 and [N31, P34, F35]CGRP 27-37 on the vasodilatation of the nasal vascular bed induced by exogenous CGRP, capsaicin, bradykinin (BK) and histamine. The attenuating effect of CGRP 8-37 analog on exogenous CGRP-induced vasodilatation, previously described in other in vivo animal models, was confirmed in the pig nasal mucosa. It also interfered with BK-and, to a lesser extent, with capsaicin-and histamine-induced decrease in vascular resistance. CGRP 27-37 analogs reduced the duration of CGRP-, capsaicin- and BK-induced vasodilatation by more than 50%. Peak values of vasodilatation were attenuated by more than 25% overall. Attenuation of histamine-induced decrease in vascular resistance was less pronounced. It is concluded that CGRP 27-37 analogs antagonize the action of exogenous CGRP, capsaicin, BK and histamine by attenuating their vasodilatation effect, both in intensity and duration. These results strongly suggest

that BK- and histamine-induced vasodilatation is partly mediated by CGRP. CGRP 8-37 and 27-37 appear to be potential contributors to the study of CGRP and its physiol. role in neurogenic inflammation. In addn., they may have putative therapeutic applications in the treatment of rhinitic patients suffering from chronic nasal obstruction.

IT 119911-68-1, 8-37-.alpha.-Calcitonin gene-related peptide (human) 224639-42-3 224639-58-1

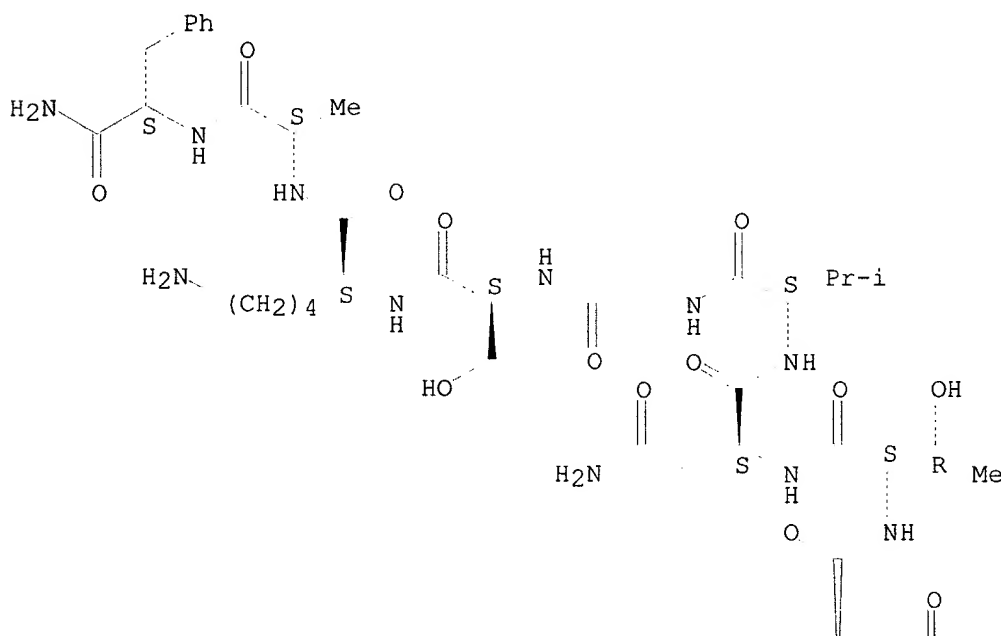
RL: PAC (Pharmacological activity); BIOL (Biological study)
(CGRP receptor antagonists modulation of nasal vasodilatory response to exogenous CGRP, capsaicin, bradykinin, and histamine)

RN 119911-68-1 CAPLUS

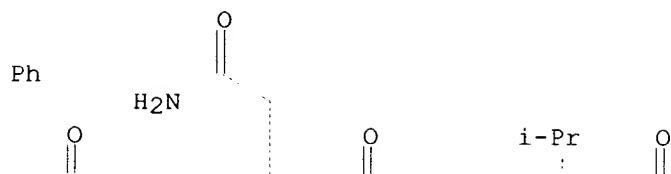
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



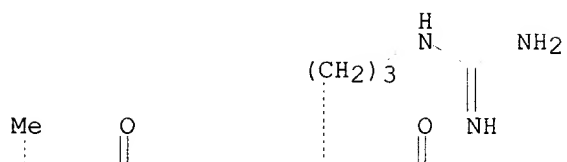
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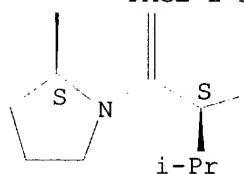
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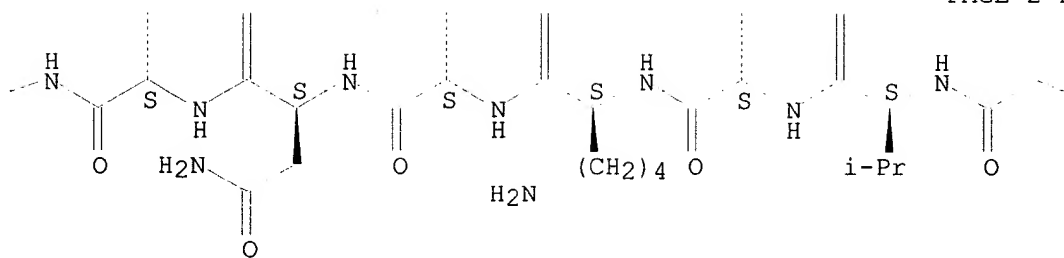
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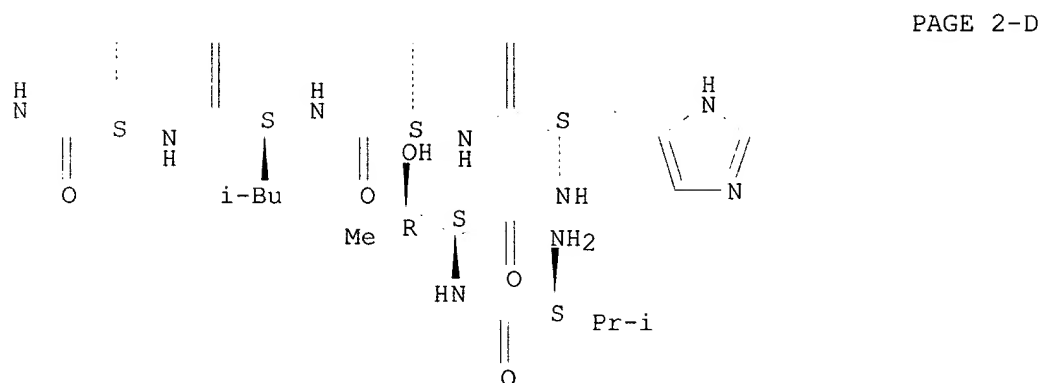
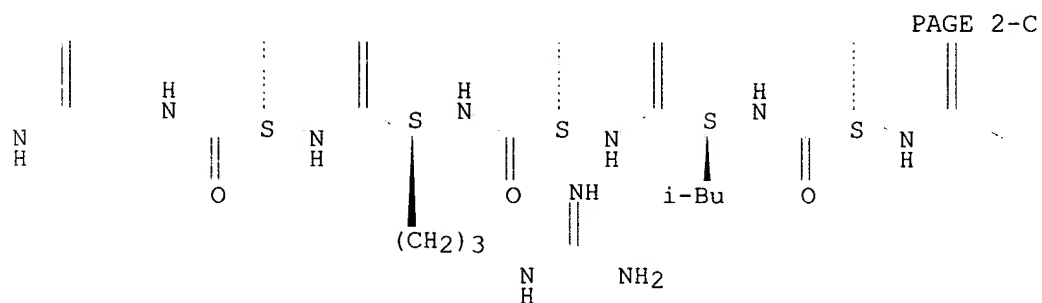


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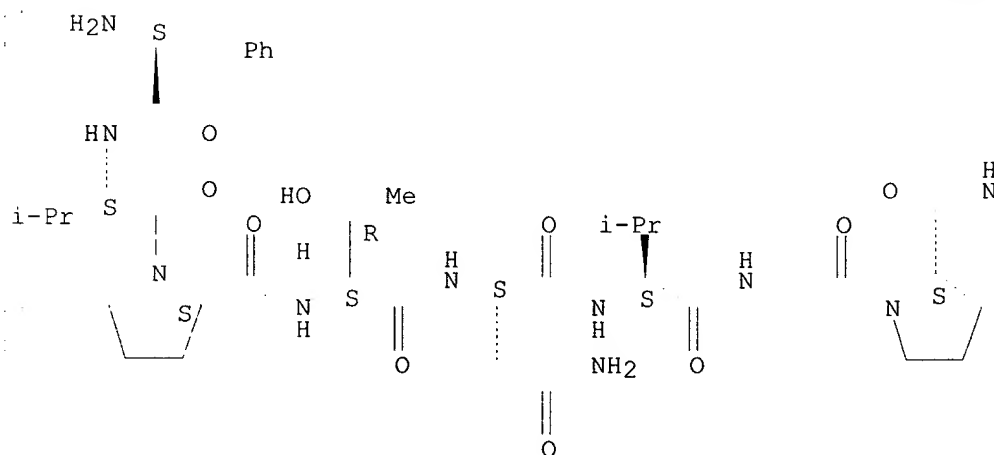


RN 224639-42-3 CAPLUS

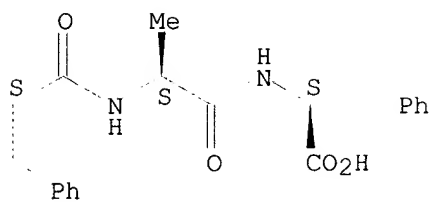
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-prolyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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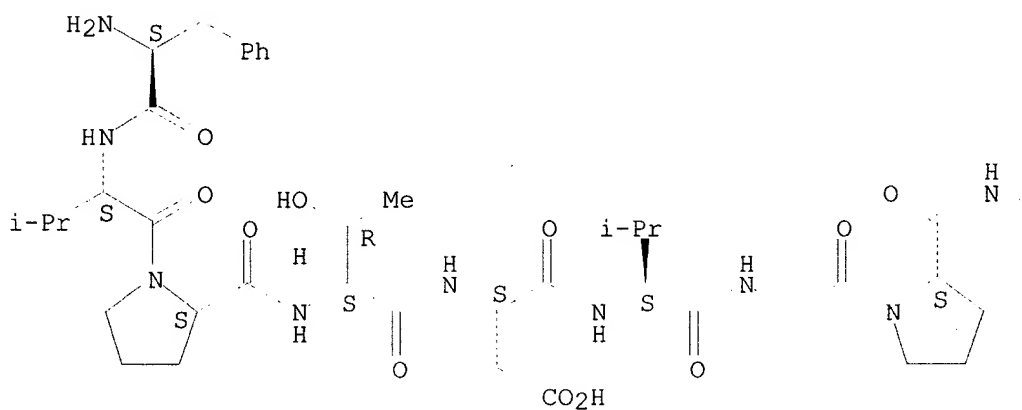


RN 224639-58-1 CAPLUS

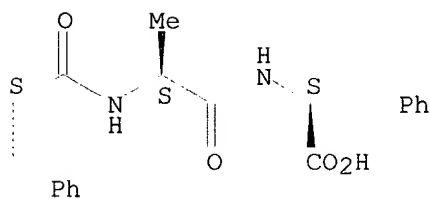
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Absolute stereochemistry.

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REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 5 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:560084 CAPLUS

DOCUMENT NUMBER: 135:153114

Searched by Barb O'Bryen, STIC 308-4291

TITLE: Preparation of peptide **antagonists** of
CGRP-receptor superfamily
INVENTOR(S): Smith, Derek David; Saha, Shankar; Abel, Peter W.
PATENT ASSIGNEE(S): Creighton University, USA
SOURCE: U.S., 24 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6268474	B1	20010731	US 1998-70504	19980430
US 2002068814	A1	20020606	US 2001-813345	20010320
PRIORITY APPLN. INFO.:			US 1998-70504	A3 19980430

OTHER SOURCE(S): MARPAT 135:153114

AB Peptides R1-X-Z [Z is a vasoactive peptide fragment of at least 15 amino acids from calcitonin gene-related peptide (CGRP); R1 is an org. group; X is CO, SO2 or (CR2R3)n, where R2 and R3 are independently H or an org. group and n is an integer 1-10] were prepd. as antagonists of CGRP. Amino terminal modification of the vasoactive peptides is done to improve their ability to bind to a member of the CGRP-receptor superfamily. Thus, N-.alpha.-benzyl-, N-.alpha.-benzoyl-, and dibenzyl-h-.alpha.- or h-.beta.-CGRP(1-37) were prepd. by the solid-phase method and data for radioligand binding and inhibition of relaxation are tabulated.

IT **119911-68-1DP**, 8-37-.alpha.-**Calcitonin gene-related peptide** (human), analogs **159435-61-7DP**, 8-37-.beta.-**Calcitonin gene-related peptide** (human), analogs **350512-72-0P**, **350512-73-1P** **350512-74-2P** **350512-75-3P**, **350512-76-4P** **350512-77-5P**

RL: **BAC (Biological activity or effector, except adverse)**; **BSU (Biological study, unclassified)**; **SPN (Synthetic preparation)**; **THU (Therapeutic use)**; **BIOL (Biological study)**; **PREP (Preparation)**; **USES (Uses)**

(prepn. of peptide **antagonists** of **CGRP-receptor** superfamily)

RN 119911-68-1 CAPLUS

CN 8-37-.alpha.-**Calcitonin gene-related peptide** (human) (9CI) (CA INDEX NAME)

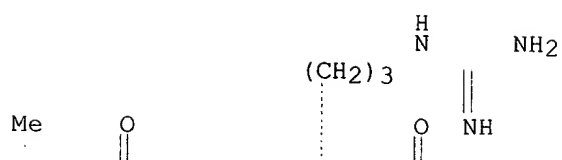
Absolute stereochemistry.

Chemical structure 10 is a complex peptide derivative. It features a long chain of amino acids with various side chains including a phenyl group (Ph), a methyl group (Me), a propyl group (Pr-i), and a hydroxyl group (OH). The structure is shown in a skeletal format with stereochemistry indicated by wedges and dashes.

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PAGE 1-D

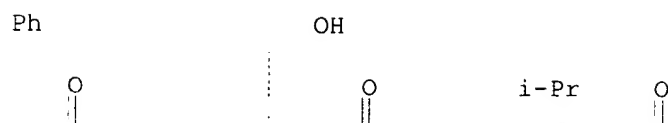


C[C@H](S1CCCC1)C(=O)N2CCCC2

The four monomers are shown as chemical structures. From left to right: 1. 2,6-pyridinedicarboxamide, a pyridine ring with amide groups at positions 2 and 6. 2. 2,6-pyridinedithione, a pyridine ring with thione groups at positions 2 and 6. 3. 2,6-pyridinedithione with a $(CH_2)_4$ chain attached to the thione group at position 2. 4. 2,6-pyridinedithione with an *i*-Pr group attached to the thione group at position 2.

Absolute stereochemistry.

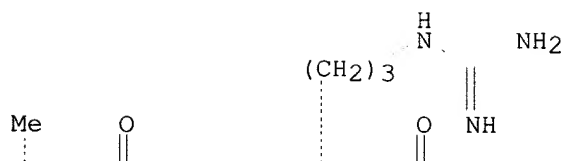
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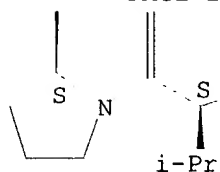
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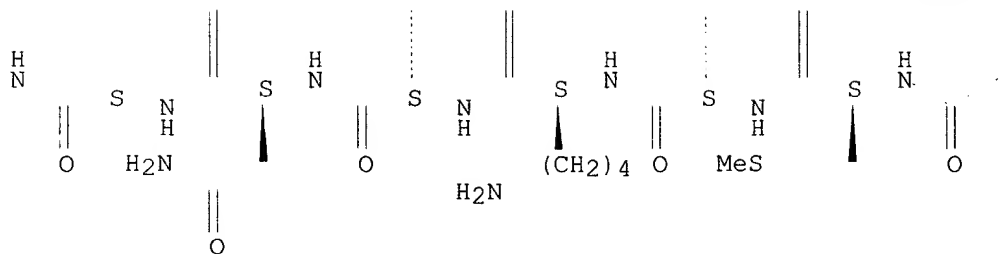
PAGE 1-D



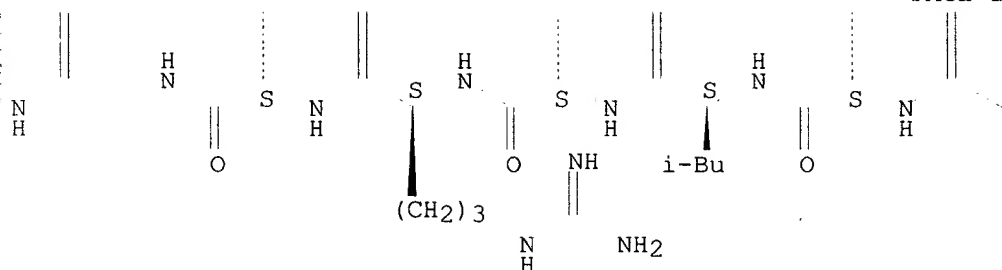
PAGE 2-A



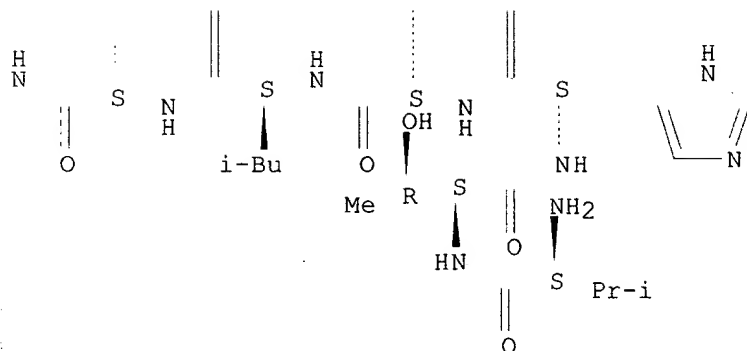
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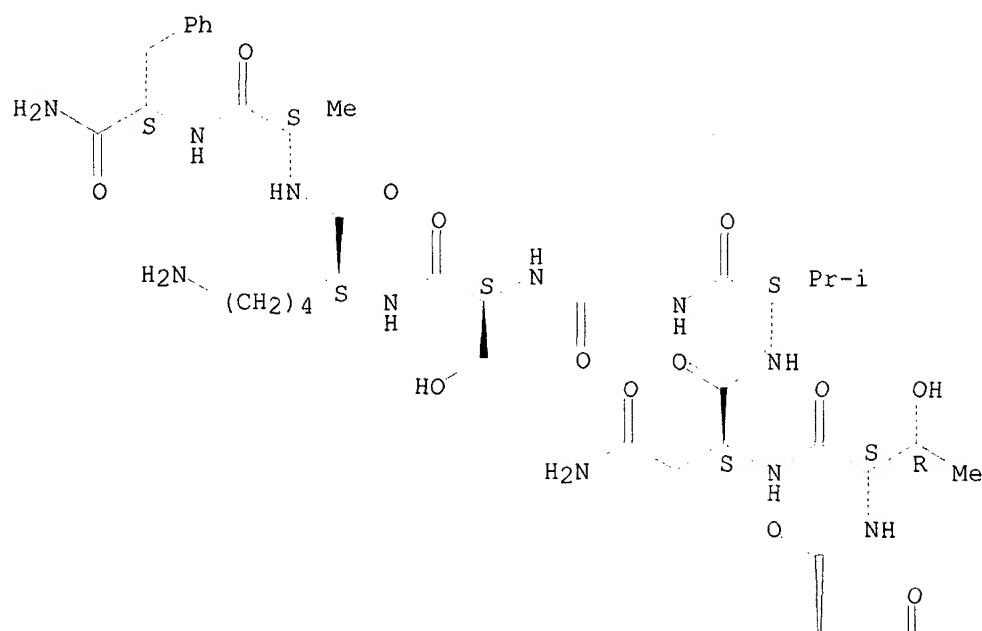
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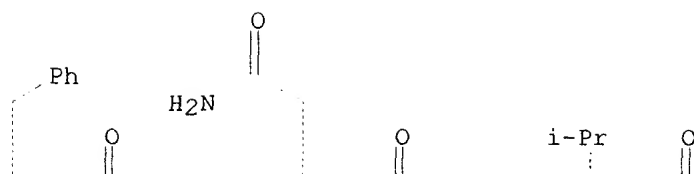
RN 350512-72-0 CAPLUS
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 serylglycylglycyl-L-valyl-L-valyl-L-lysyl-L-asparaginyl-L-asparaginyl-L-
 phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-
 seryl-L-lysyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



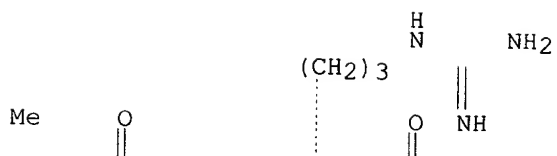
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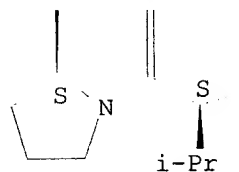
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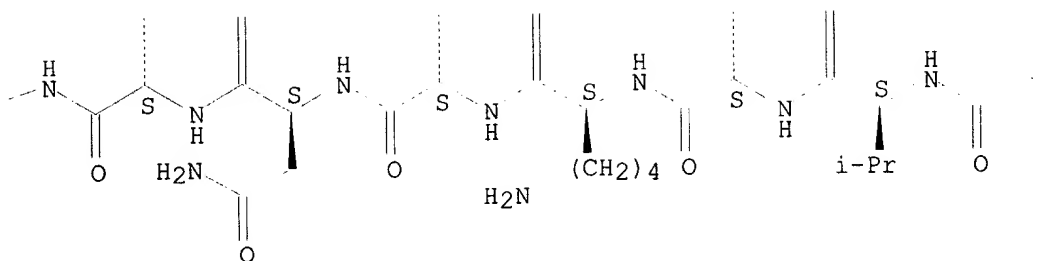
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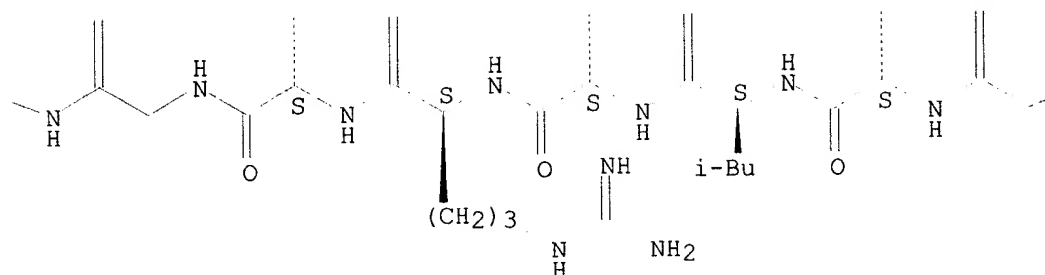
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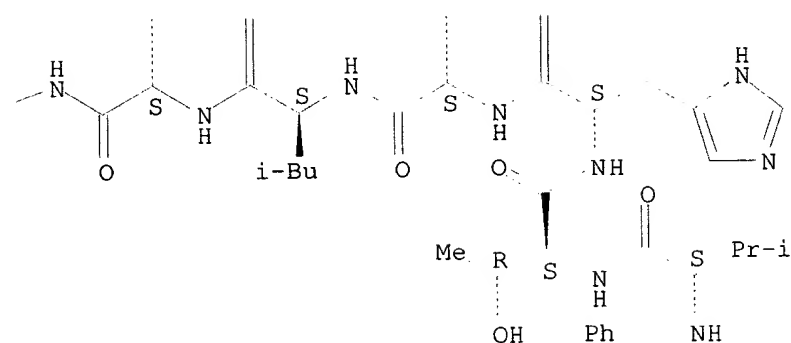
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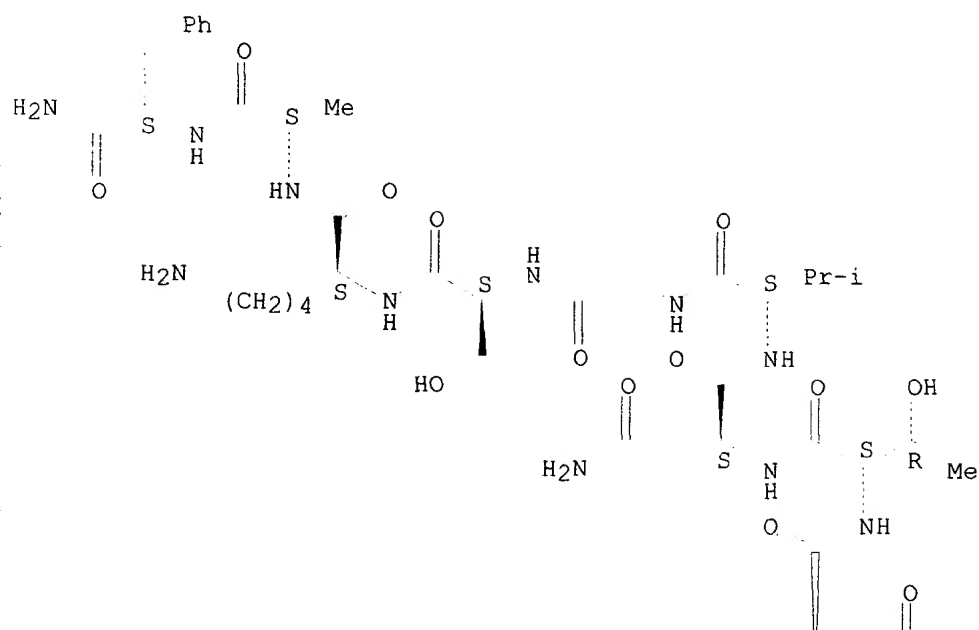
PAGE 2-D



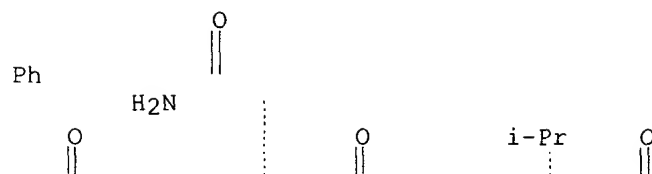
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Absolute stereochemistry.

PAGE 1-A



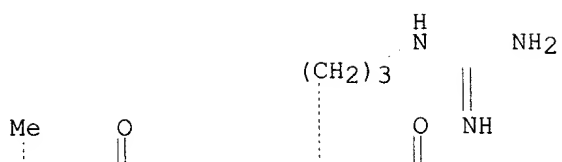
PAGE 1-B



PAGE 1-C



PAGE 1-D



N[C@@H](CCCCNC(=O)NCCSCC(N)=O)[C@H](O)CCCNC(=O)NCCSCC(N)=O

Chemical structures of the following compounds are shown:

The structures are:

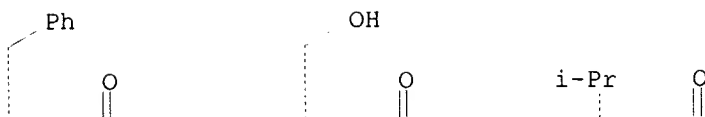
- (I) 1,2,3,4-tetrahydro-6-methyl-5H-benzothiazine-5-thione
- (II) 1,2,3,4-tetrahydro-6-methyl-5H-benzothiazine-5-thione
- (III) 1,2,3,4-tetrahydro-6-methyl-5H-benzothiazine-5-thione

L-Phenylalaninamide, N-(phenylmethyl)-L-valyl-L-threonyl-L-histidyl-L-arginyl-L-leucyl-L-alanylglycyl-L-leucyl-L-leucyl-L-seryl-L-arginyl-L-serylglycylglycyl-L-methionyl-L-valyl-L-lysyl-L-seryl-L-asparaginyl-L-

Absolute stereochemistry.

Chemical structure 1 is a complex peptide derivative. It features a central backbone with various side chains. The structure includes amide bonds, a thioether linkage, and a hydroxyl group. Stereochemistry is indicated with wedges and dashes.

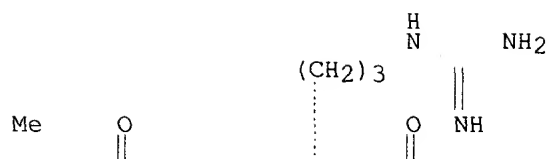
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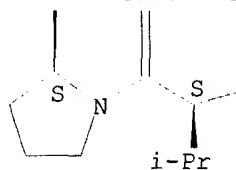
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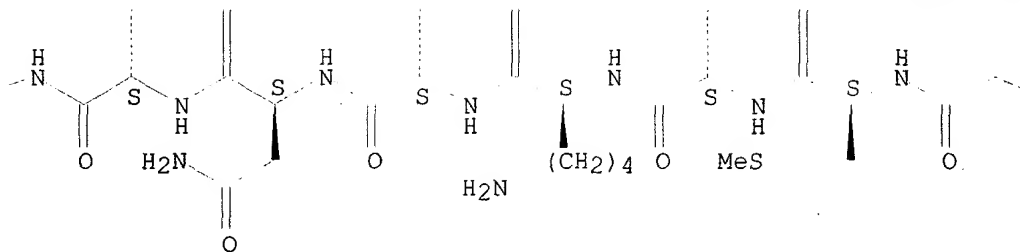
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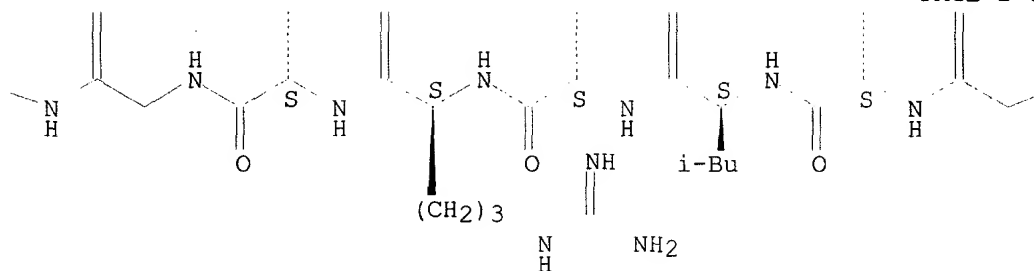
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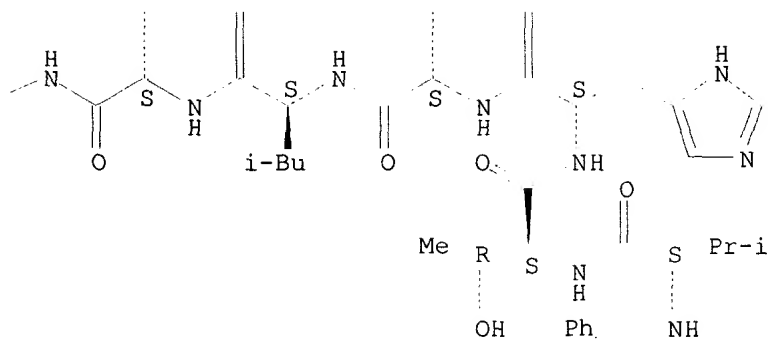
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PAGE 2-C

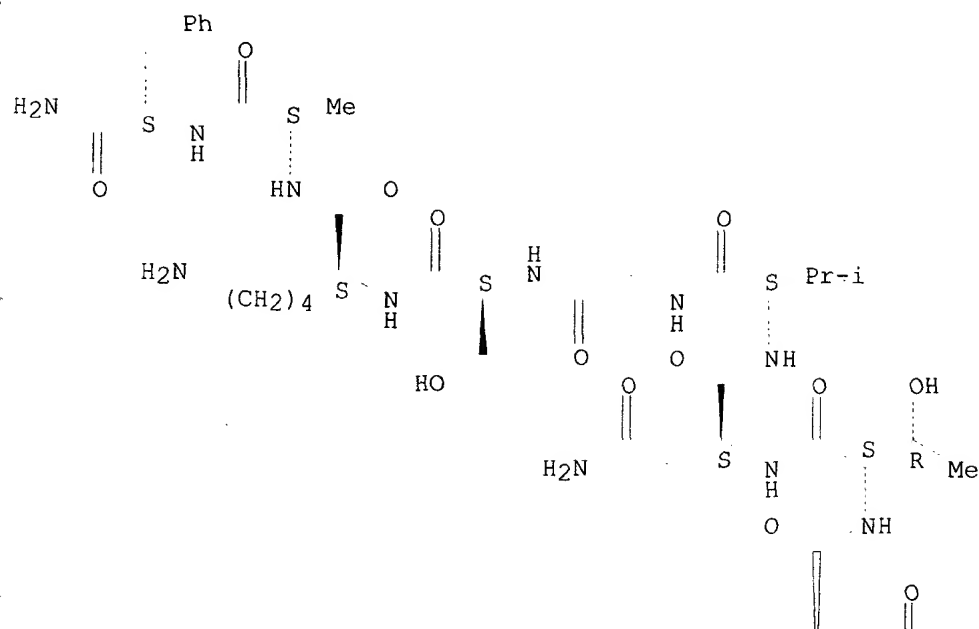


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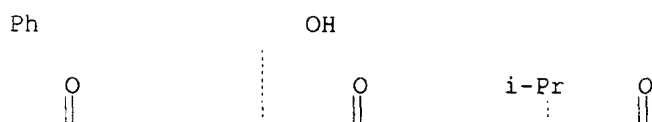


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PAGE 1-A



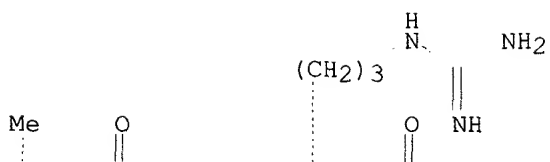
PAGE 1-B



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PAGE 1-D



Chemical structures of the polymers are shown in Figure 1. The polymers were prepared by the reaction of the corresponding diisocyanate with the diamine in the presence of triethylamine as catalyst. The polymers were characterized by elemental analysis, infrared, and ¹H NMR spectroscopy. The molecular weights were determined by gel permeation chromatography (GPC) using polystyrene as standards. The polymers were characterized by their inherent viscosities in dimethyl sulfoxide (DMSO) at 30°C. The polymers were characterized by their thermal stability in nitrogen and air atmospheres by thermogravimetric analysis (TGA). The polymers were characterized by their glass transition temperatures (T_g) by differential scanning calorimetry (DSC).

[illegible]

Chemical structures of the following compounds are shown:

1,2,3,4-tetrahydro-6-methyl-5H-benzothiazine-5-thione (1)

1,2,3,4-tetrahydro-6-methyl-5H-benzothiazine-5-thione (2)

1,2,3,4-tetrahydro-6-methyl-5H-benzothiazine-5-thione (3)

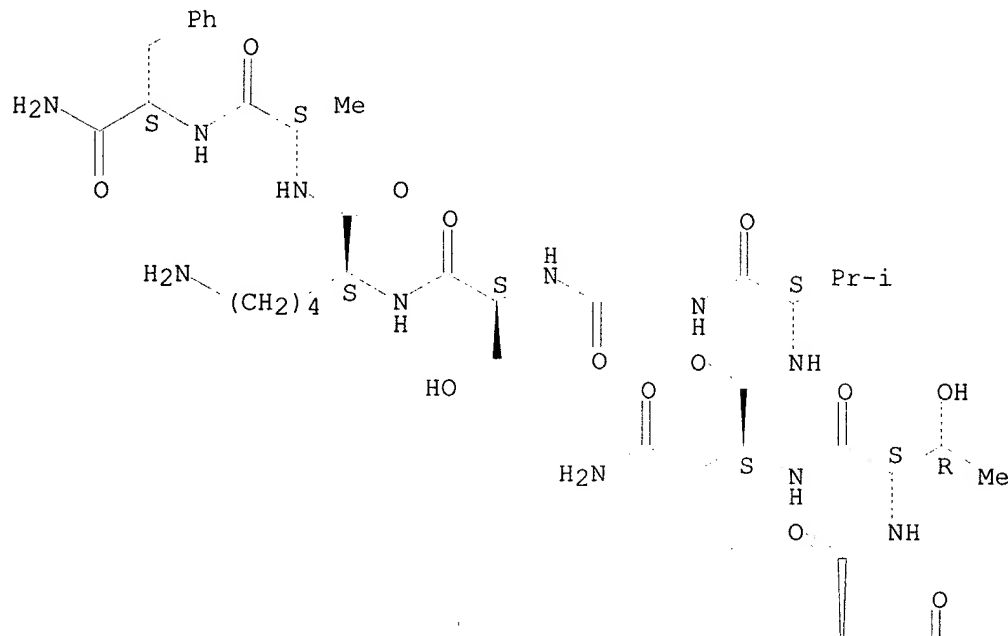
1,2,3,4-tetrahydro-6-methyl-5H-benzothiazine-5-thione (4)

Searched by Barb O'Bryen, STIC 308-4291

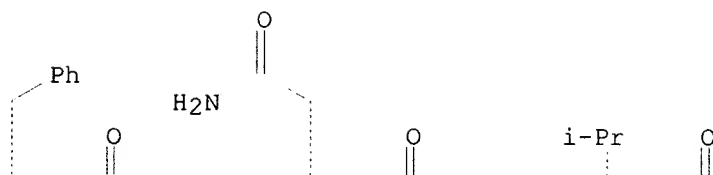
phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyL-L-valylglycyl-L-seryl-L-lysyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



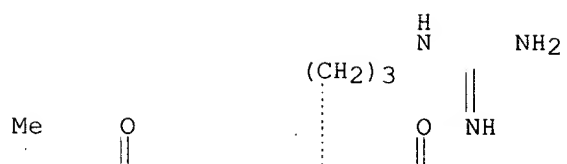
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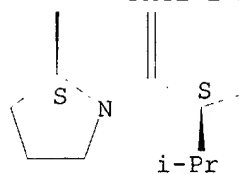
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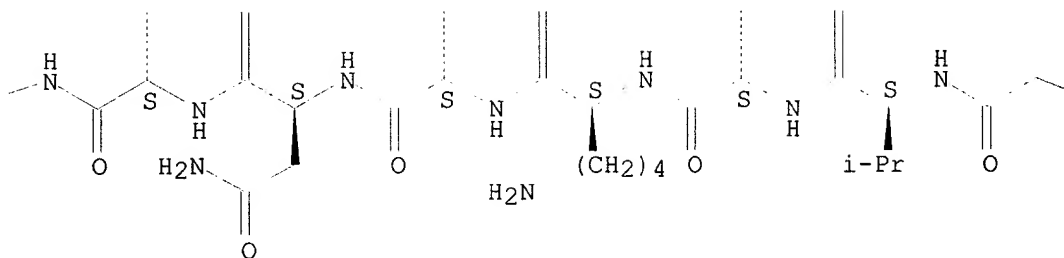
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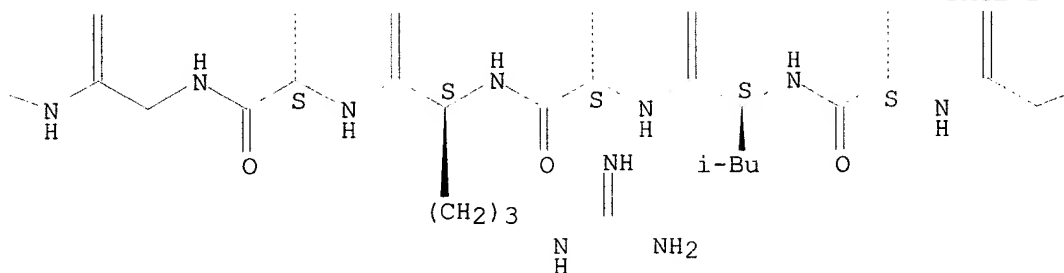
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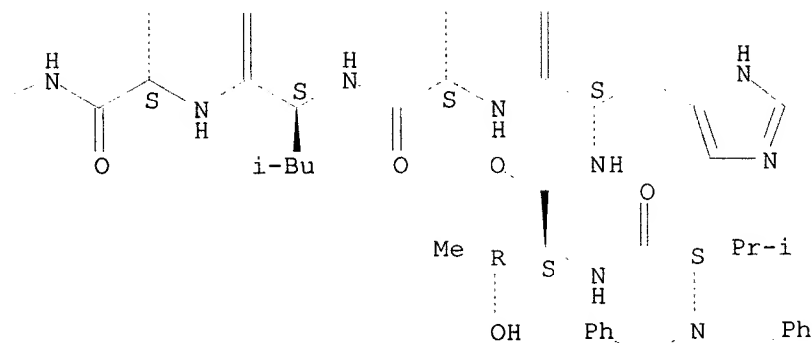
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PAGE 2-C



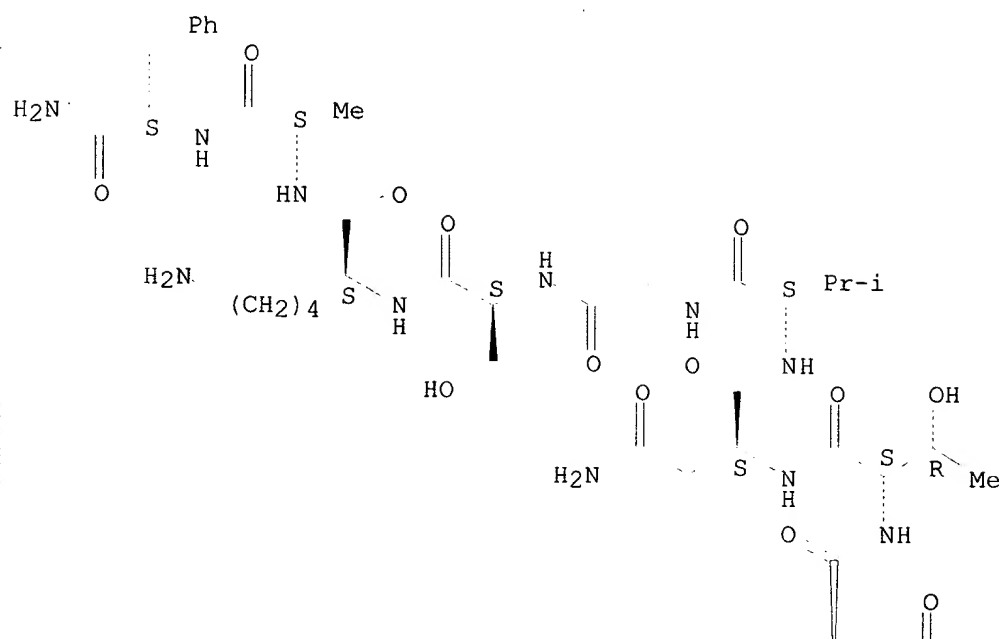
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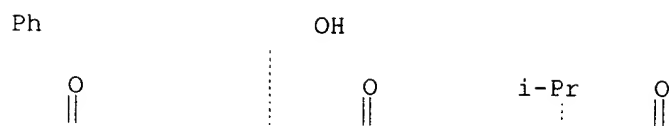
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 phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-
 seryl-L-lysyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



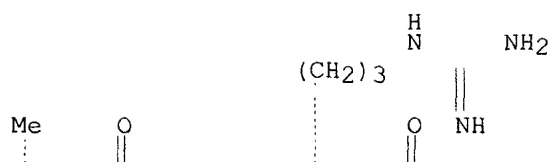
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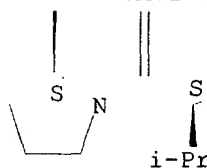
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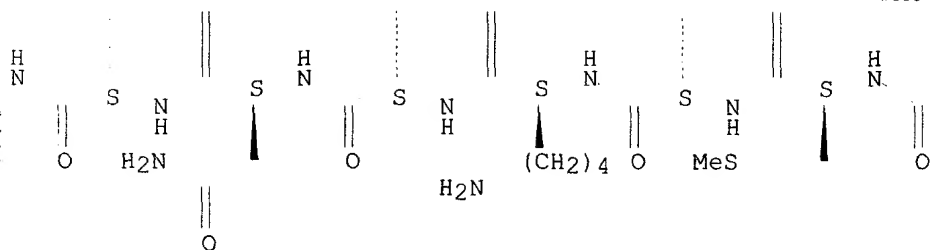
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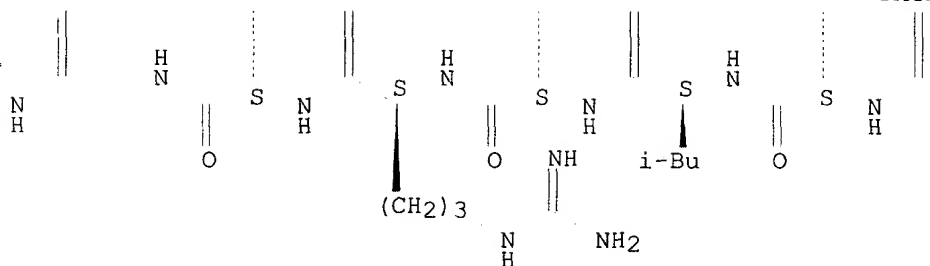
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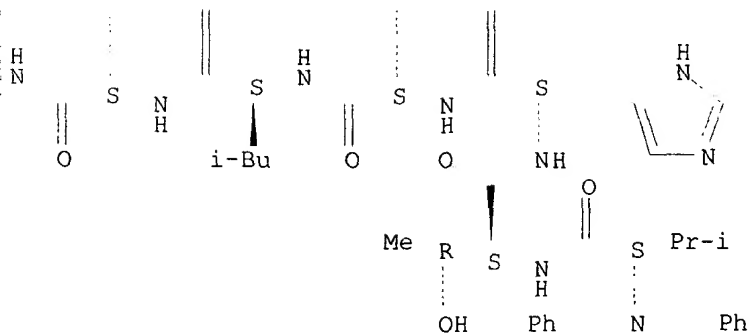
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PAGE 2-D



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 6 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:164211 CAPLUS
DOCUMENT NUMBER: 135:40865

Searched by Barb O'Bryen, STIC 308-4291

TITLE: Characterisation of the effects of a non-peptide
CGRP receptor antagonist
in SK-N-MC cells and isolated human cerebral arteries
AUTHOR(S): Edvinsson, L.; Sams, A.; Jansen-Olesen, I.; Tajti, J.;
Kane, S. A.; Rutledge, R. Z.; Koblan, K. S.; Hill, R.
G.; Longmore, J.
CORPORATE SOURCE: Department of Internal Medicine, Lund University
Hospital, Lund, S-22185, Swed.
SOURCE: European Journal of Pharmacology (2001), 415(1), 39-44
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The cerebral circulation is innervated by calcitonin gene-related peptide (CGRP) contg. fibers originating in the trigeminal ganglion. During a migraine attack, there is a release of CGRP in conjunction with the head pain, and triptan administration abolishes both the CGRP release and the pain at the same time. In the search for a novel treatment of migraine, a non-peptide CGRP antagonist has long been sought. Here, we present data on a human cell line and human and guinea-pig isolated cranial arteries for such an antagonist, (4-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)piperidine-1-carboxylic acid [1-(3,5-dibromo-4-hydroxy-benzyl)-2-oxo-2-(4-phenyl-piperazin-1-yl)ethyl]amide) (I). On SK-N-MC cell membranes, radiolabeled CGRP binding was displaced by both CGRP-(8-37) and I, yielding pKi values of 8.9 and 7.8, resp. Functional studies with SK-N-MC cells showed that CGRP-induced cAMP prodn. was antagonized by both CGRP-(8-37) and I with pA2 values of 7.8 and 7.7, resp. Isolated human and guinea pig cerebral arteries were studied with a sensitive myograph technique. CGRP induced a concn.-dependent relaxation in human cerebral arteries which was antagonized by both CGRP-(8-37) and I in a competitive manner. In guinea pig basilar arteries, CGRP-(8-37) antagonized the CGRP-induced relaxation while I had a weak blocking effect. The clin. studies of non-peptide CGRP antagonists are awaited with great interest.

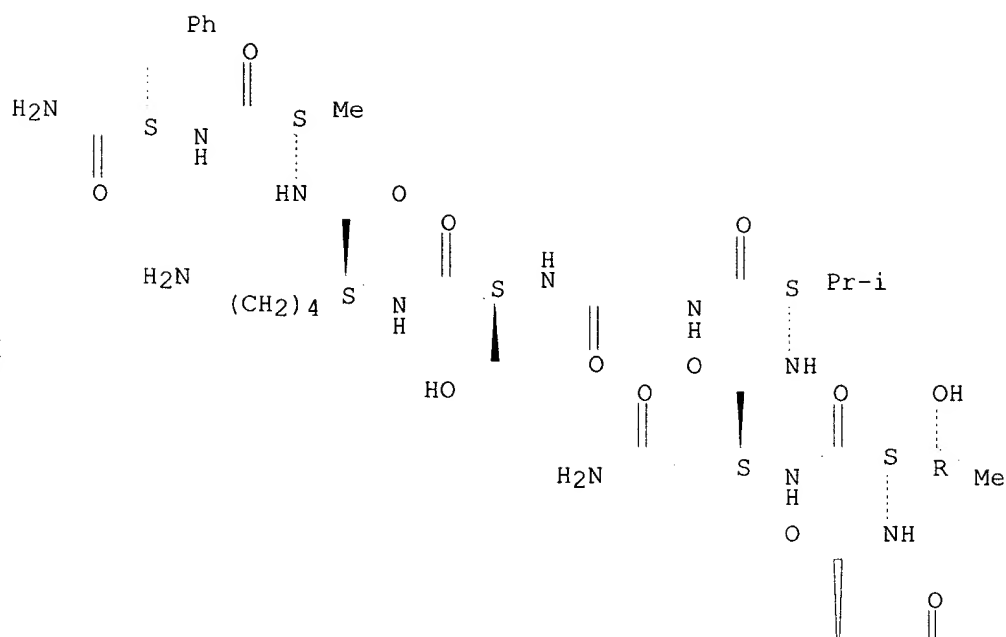
IT 119911-68-1, human CGRP(8-37)
RL: BAC (Biological activity or effector, except adverse); BSU
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human cerebral arteries)

RN 119911-68-1 CAPLUS

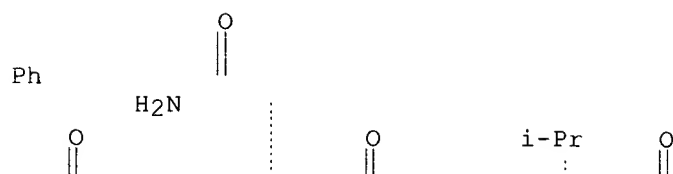
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

PAGE 1-A



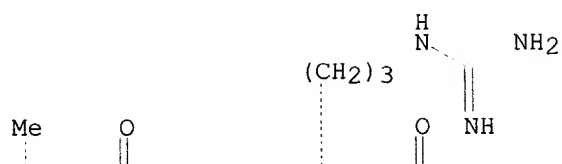
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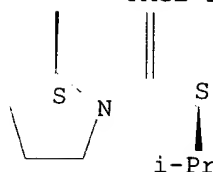
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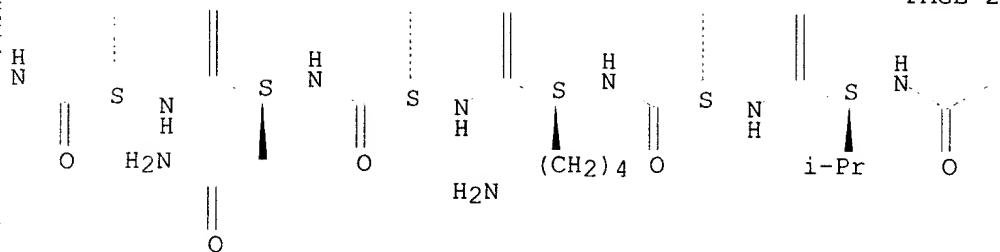
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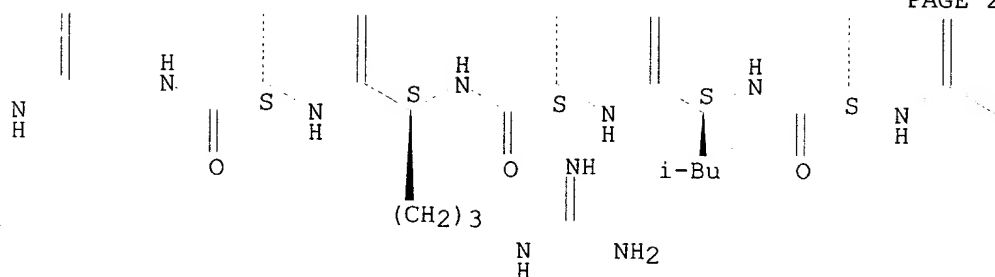
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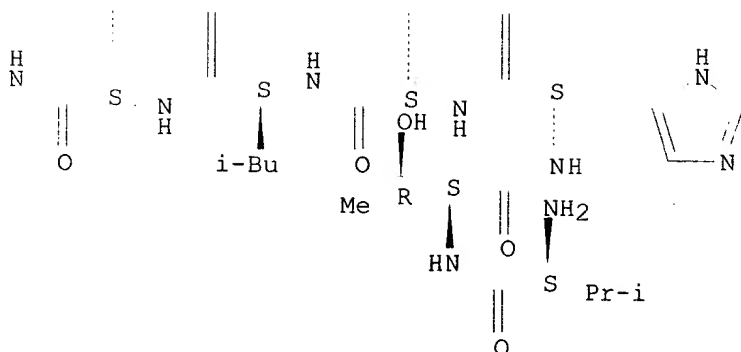
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REFERENCE COUNT:

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THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 7 OF 48

CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2000:894620 CAPLUS

DOCUMENT NUMBER:

134:141358

Searched by Barb O'Bryen, STIC 308-4291

TITLE: Development of the first **CGRP-antagonist** with nanomolar affinity

AUTHOR(S): Beck-Sickinger, Annette G.; Rist, Beate; Enzeroth, Michael; Lacroix, Silvain

CORPORATE SOURCE: Department of Pharmacy, ETH Zurich, Zurich, CH 8057, Switz.

SOURCE: Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 222-223. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Kluwer Academic Publishers: Dordrecht, Neth.
CODEN: 69ATHX

DOCUMENT TYPE: Conference

LANGUAGE: English

AB CGRP 27-37, which binds to human CGRP1-receptors with low affinity, has been systematically varied. In a stepwise rational optimization the undcapeptides FVPTNVGPFAF and FVPTDVGPFAF have been identified, which bind to human CGRP-receptors. The replacement of Ser34 by Pro has turned out to be crucial for the increase of affinity. Interestingly, neither hydroxyproline (Hyp), nor homoproline (Hpr) could fully replace Pro34, whereas Aib and Tic were only slightly less active. The increase of affinity of single mutations has been additive and correlated with the decrease of the min. at $\lambda_{\text{max}} = 220 \text{ nm}$ by CD spectroscopy. FVPTDVGPFAF and FVPTNVGPFAF showed exclusively antagonistic properties in the rat vasodilatation assay. Interestingly, the duration of the potency of both compds. varied significantly. Whereas FVPTDVGPFAF lost potency after 30 min, analogs with replacement of Asp31 by Asn31 were active for more than 2 h. Since both ligands exhibit receptor binding affinities in the same range ($K_i = 19/14 \text{ nM}$), the authors suggested that the analog with Asp31 is more rapidly metabolized, perhaps because of an increased susceptibility for proteases. This effect could be confirmed by preliminary results with other analogs contg. either Asp or Asn in position 31. In this case as well, the effect of the Asp contg. peptides was significantly increased. This suggests differences in the metab. of both compds. and could be important for drug design.

IT 224639-29-6 224639-36-5 224639-42-3
224639-47-8 224639-53-6 224639-58-1
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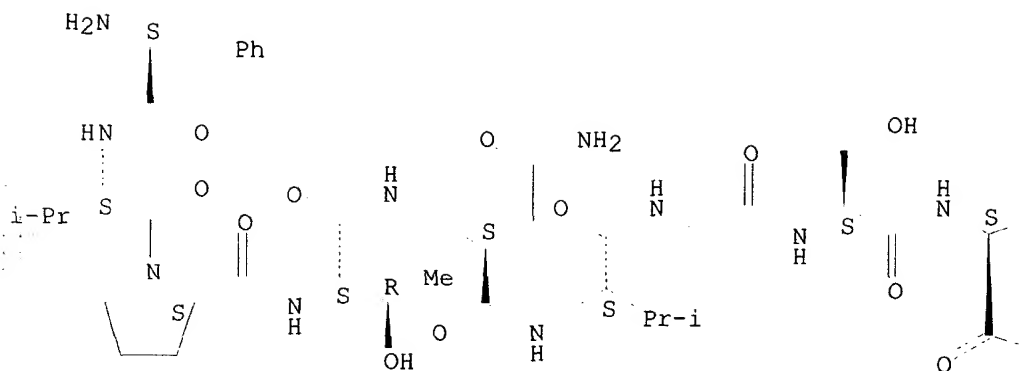
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(development of first **CGRP-antagonist** with nanomolar affinity)

RN 224639-29-6 CAPLUS

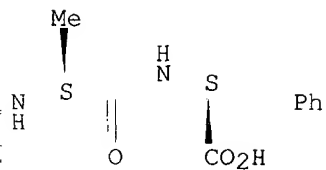
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Absolute stereochemistry.

PAGE 1-A



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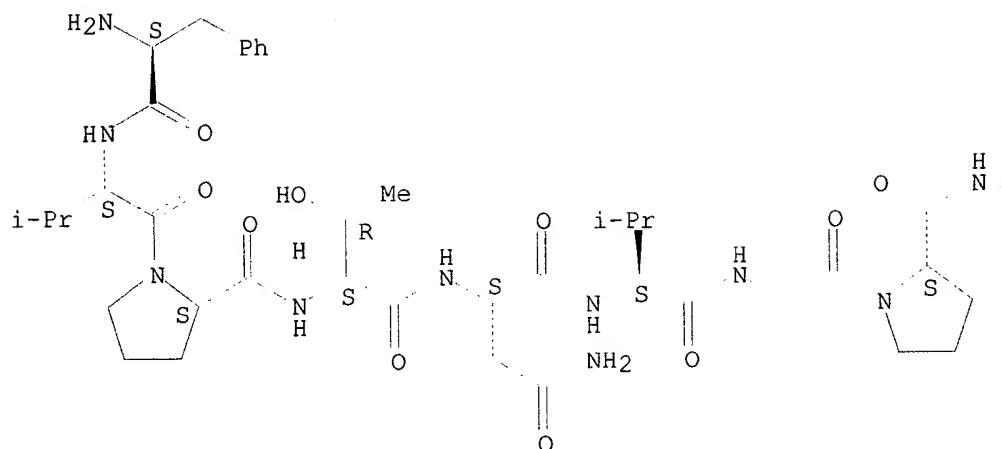
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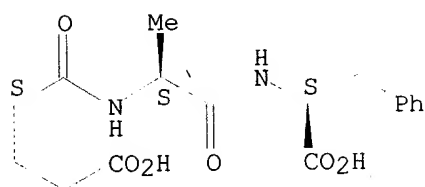
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Absolute stereochemistry.

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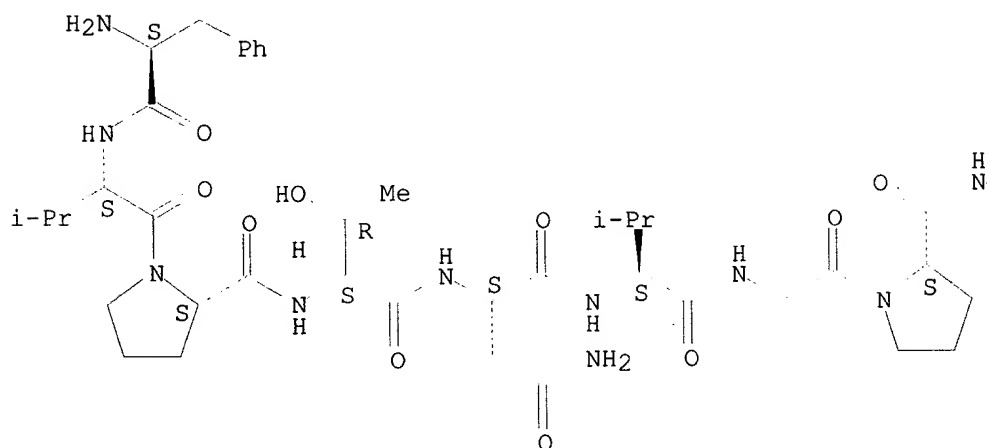
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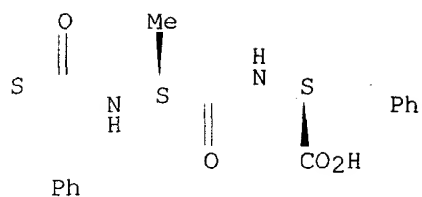
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Absolute stereochemistry.

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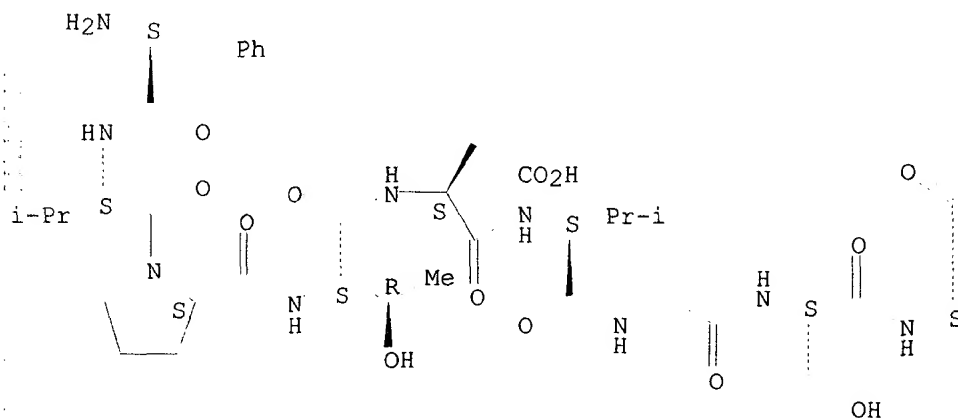


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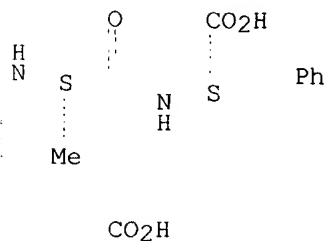
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INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

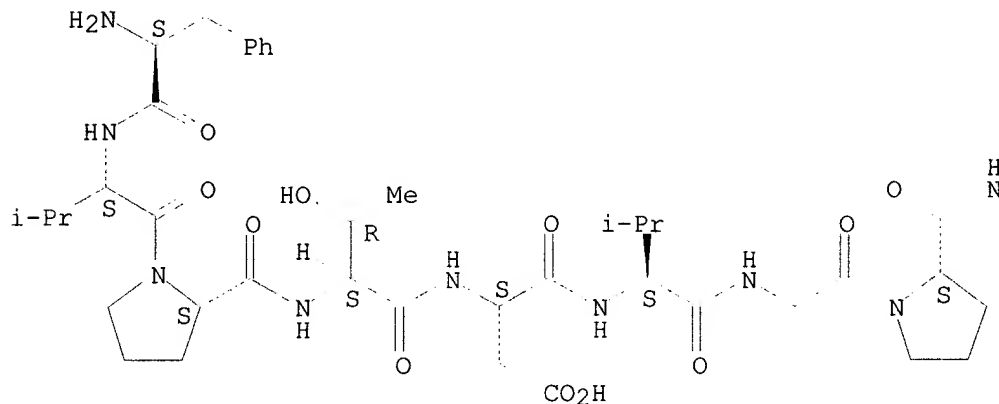


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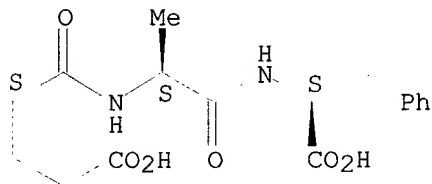
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INDEX NAME)

Absolute stereochemistry.

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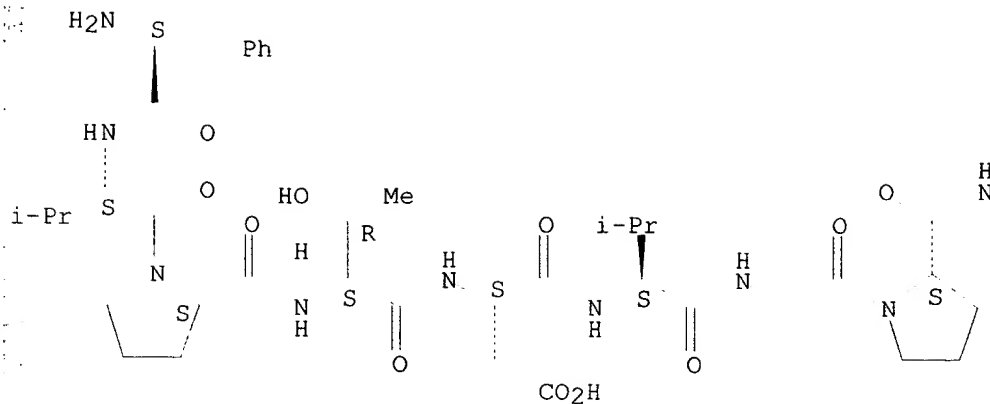


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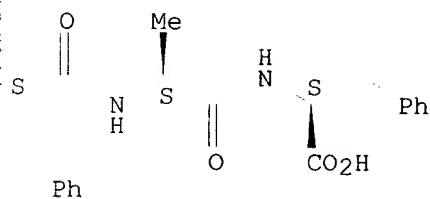
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NAME)

Absolute stereochemistry.

PAGE 1-A



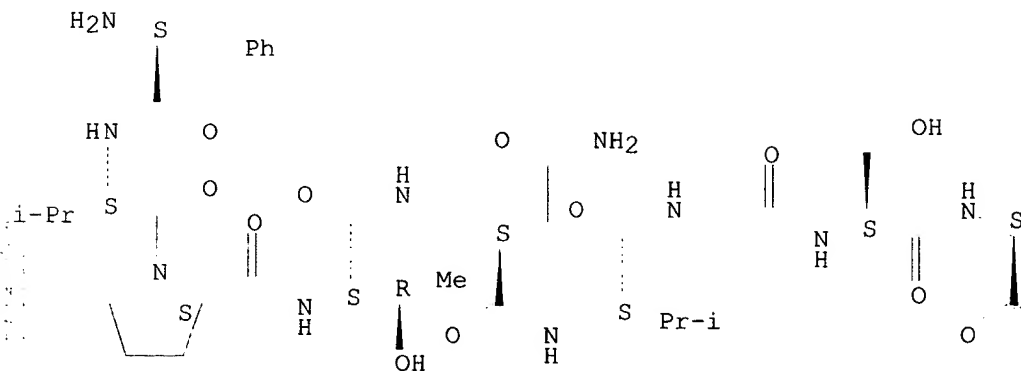
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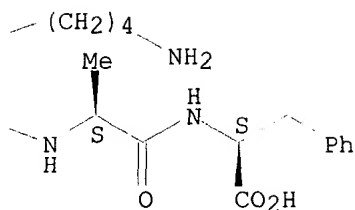
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Absolute stereochemistry.

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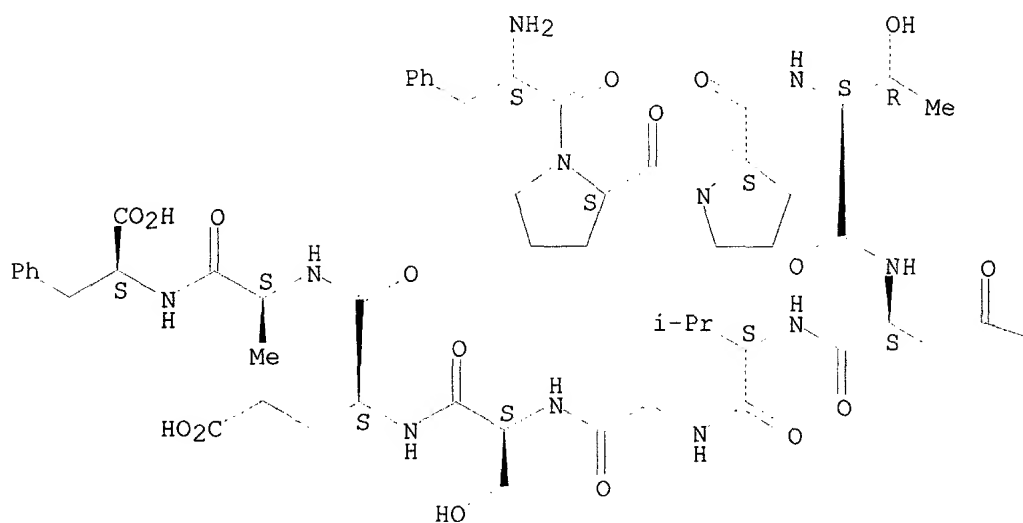


RN 324035-50-9 CAPLUS

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Absolute stereochemistry.

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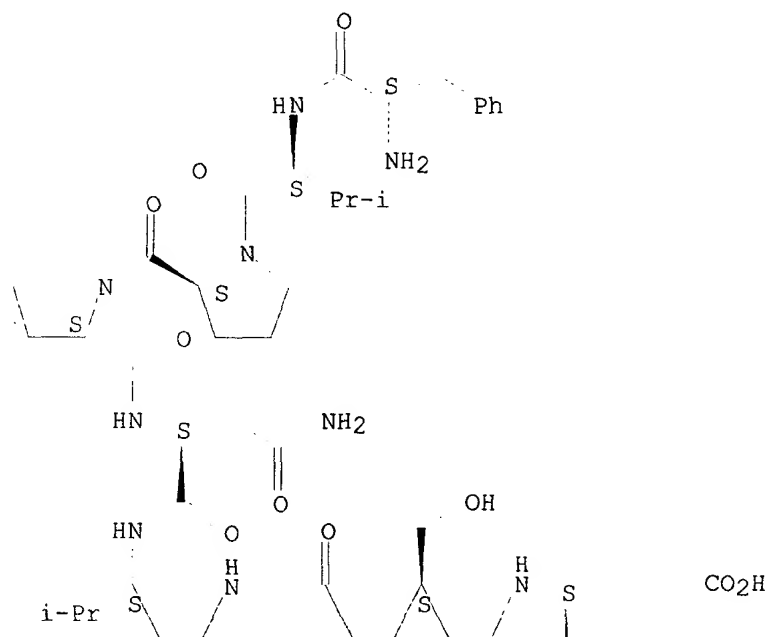
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RN 324035-51-0 CAPLUS

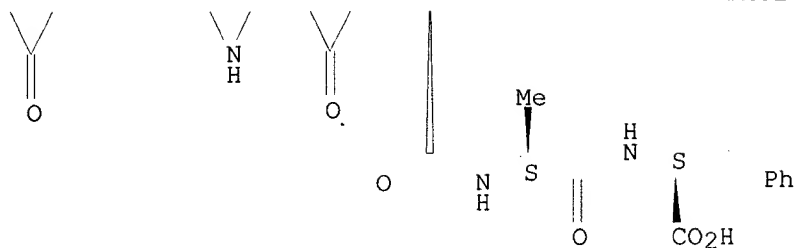
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-prolyl-L-asparaginyl-L-valylglycyl-L-seryl-L- α -glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



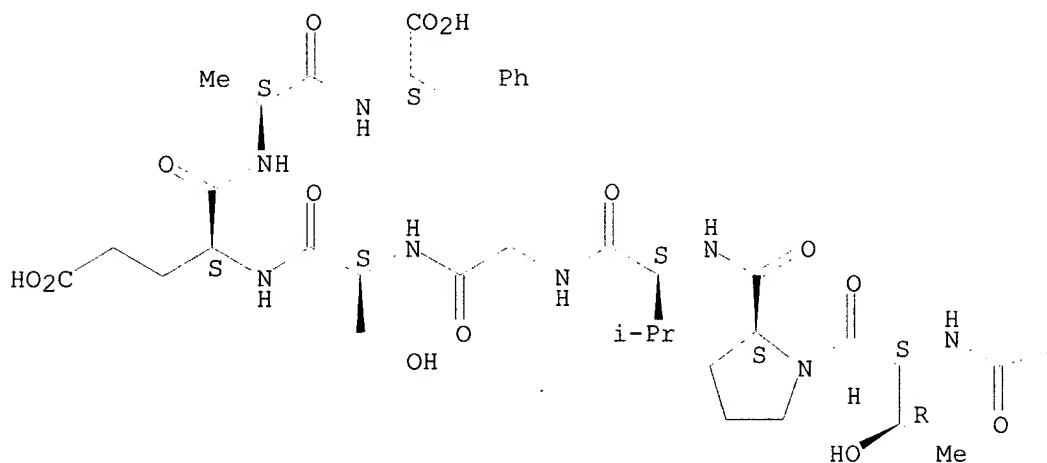
PAGE 2-A



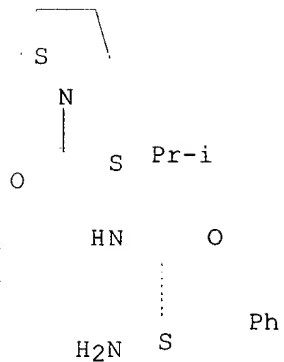
RN 324035-52-1 CAPLUS
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-prolyl-L-valylglycyl-L-seryl-L-.alpha.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



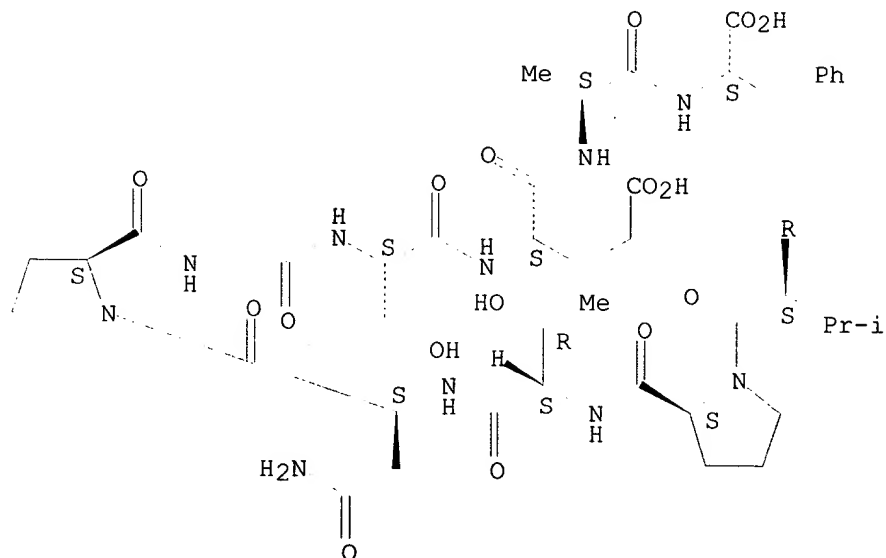
PAGE 1-B



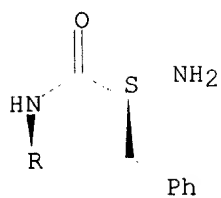
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Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

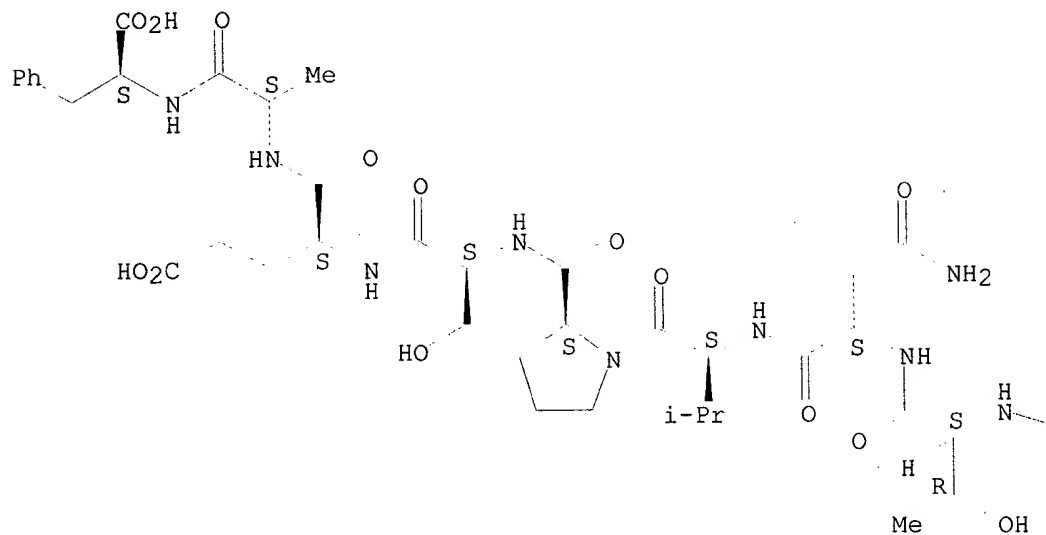


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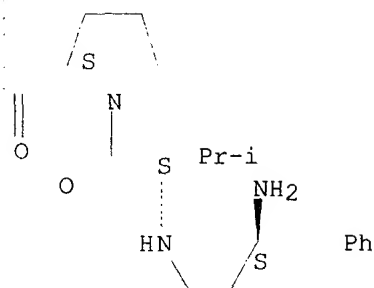
RN 324033-34-3 CAPLOS
CN L-Phenylalanyne, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valyl-L-prolyl-L-seryl-L-.alpha.-glutamyl-L-alanyl-; (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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PAGE 1-B



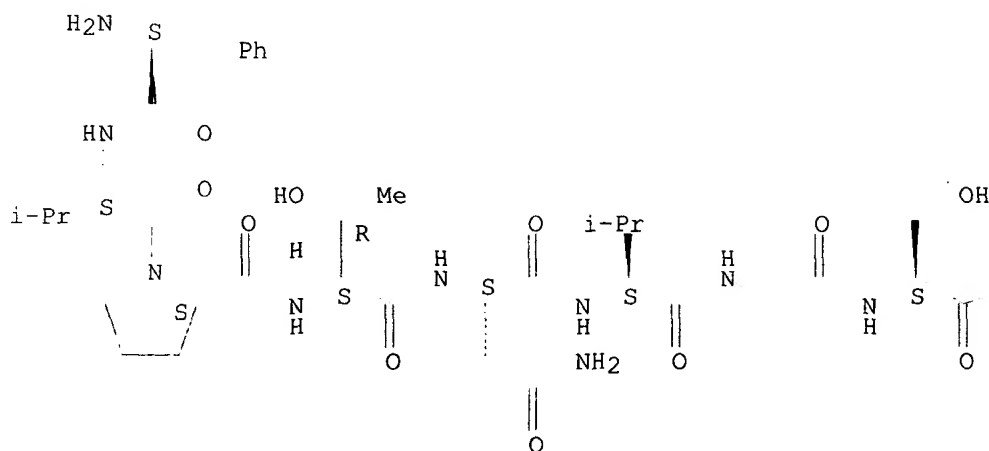
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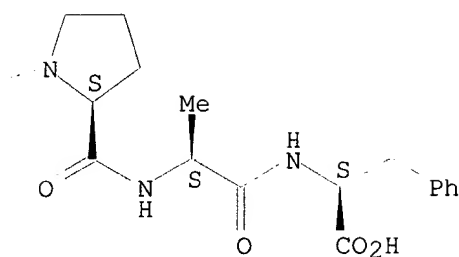
RN 324035-55-4 CAPLUS
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-prolyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

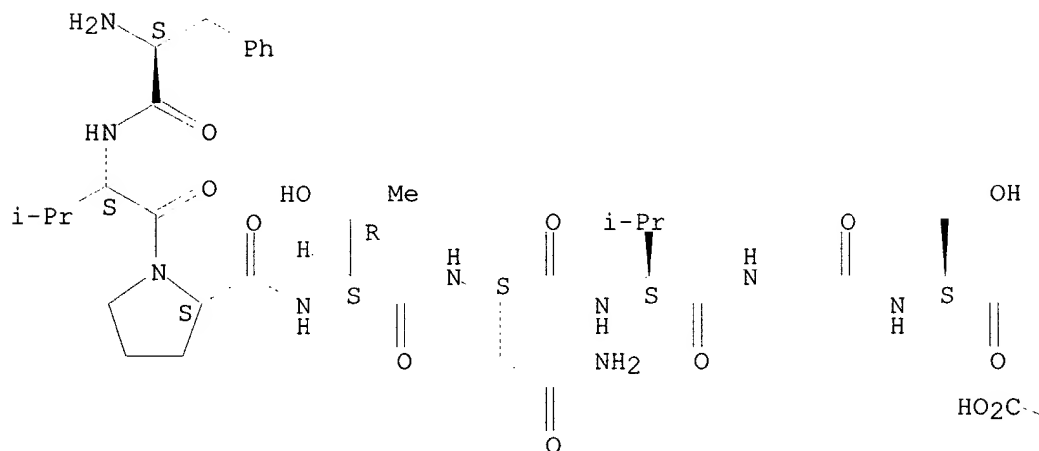


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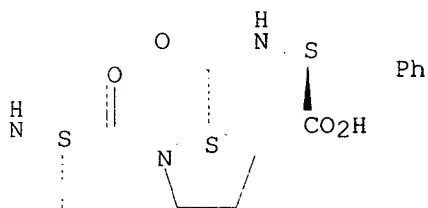
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyll-L-valylglycyl-L-seryl-L-.alpha.-glutamyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



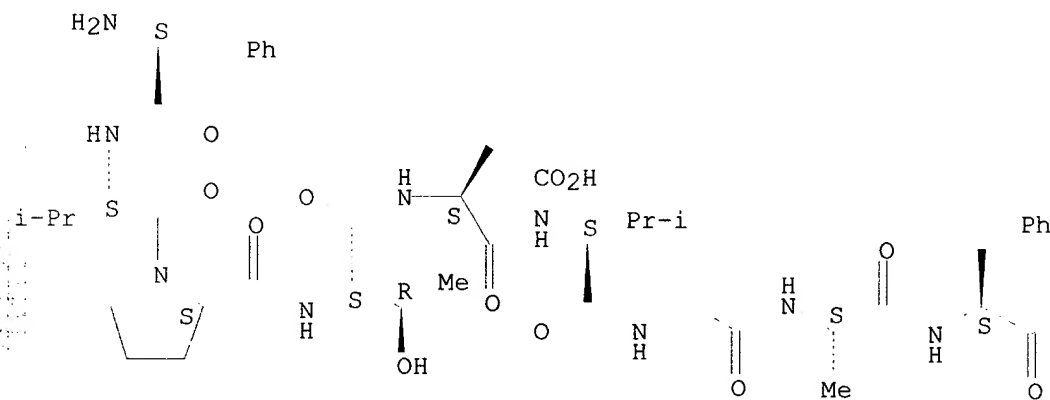
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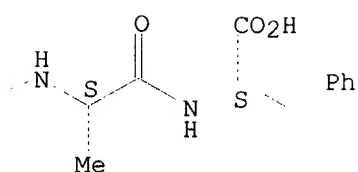
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aspartyl-L-valylglycyl-L-alanyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

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PAGE 1-B

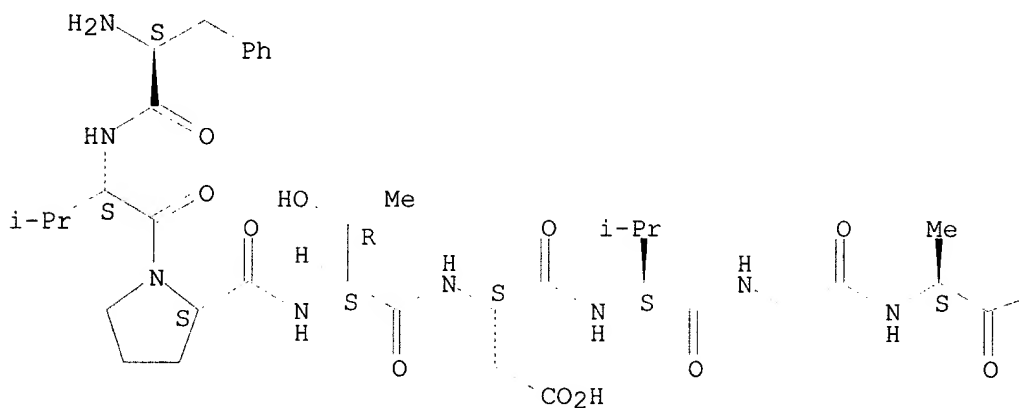


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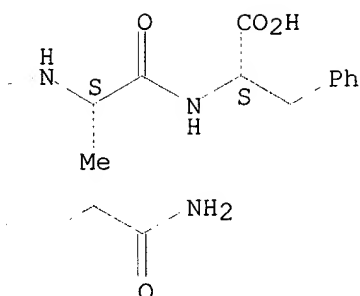
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-aspartyl-L-valylglycyl-L-alanyl-L-histidyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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PAGE 1-B

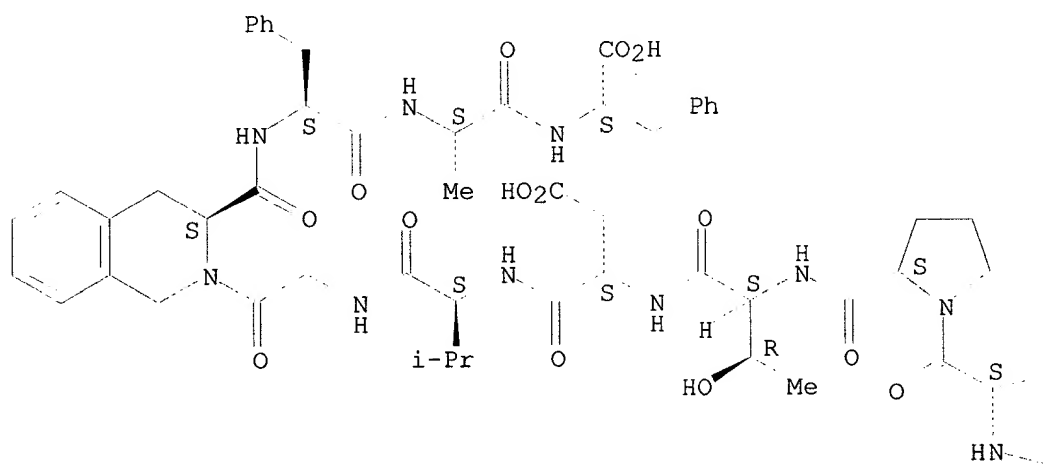


RN 324035-60-1 CAPLUS

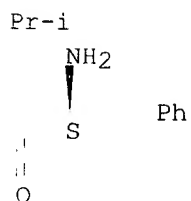
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
aspartyl-L-valylglycyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-
phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



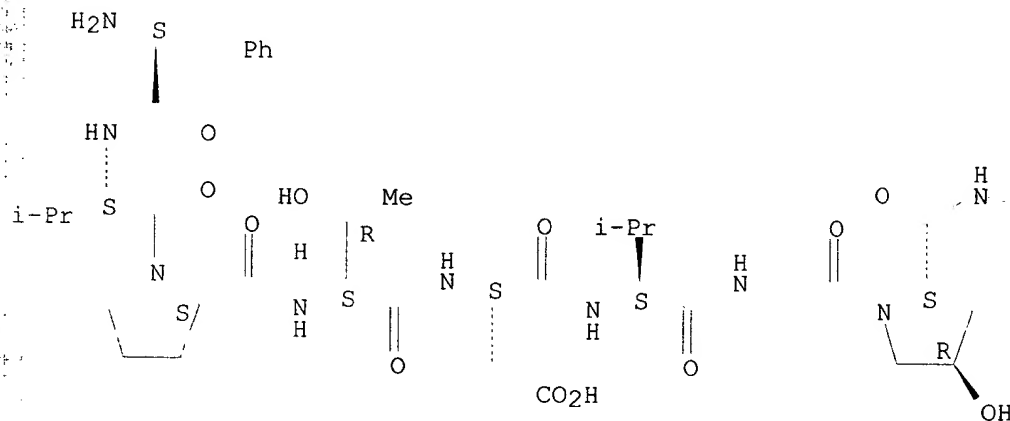
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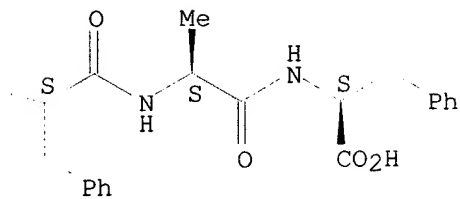
RN 324035-61-2 CAPLUS
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
aspartyl-L-valylglycyl-(4R)-4-hydroxy-L-prolyl-L-phenylalanyl-L-alanyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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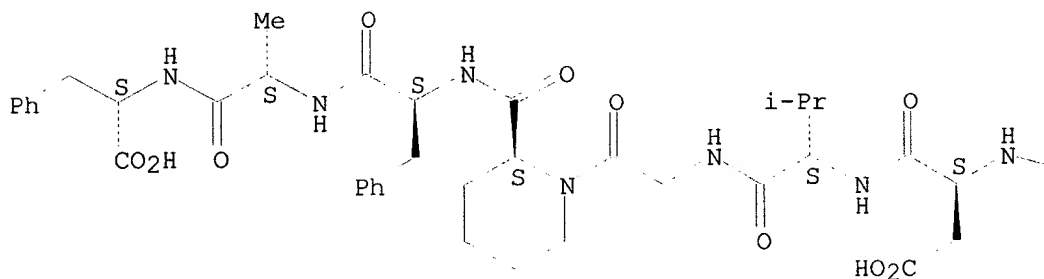


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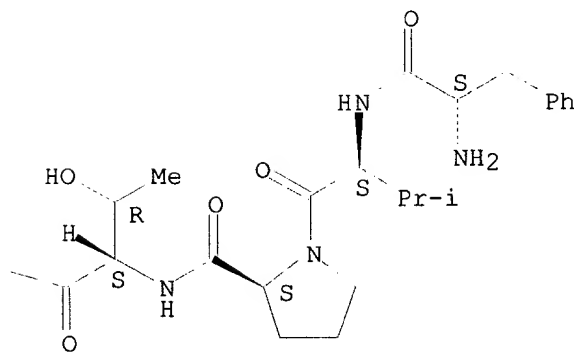
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
aspartyl-L-valylglycyl-(2S)-2-piperidinecarbonyl-L-phenylalanyl-L-alanyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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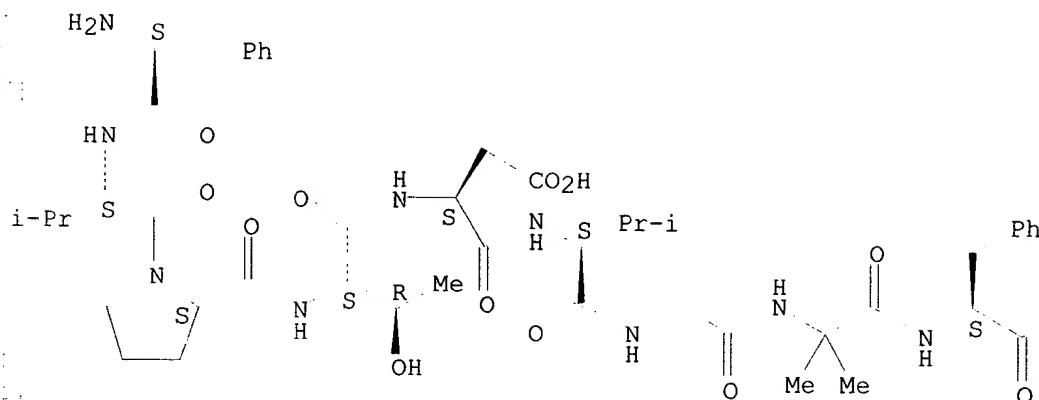


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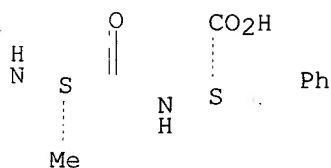
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
aspartyl-L-valylglycyl-2-methylalanyl-L-phenylalanyl-L-alanyl- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 8 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:613482 CAPLUS

DOCUMENT NUMBER: 133:247659

TITLE: Adrenomedullin inhibits spontaneous and bradykinin-induced but not oxytocin- or prostaglandin F₂.alpha.-induced periodic contraction of rat uterus
AUTHOR(S): Yanagita, Toshihiko; Yamamoto, Ryuichi; Sugano, Takashi; Kobayashi, Hideyuki; Uezono, Yasuhito; Yokoo, Hiroki; Shiraishi, Seiji; Minami, Shin-Ichi; Wada, Akihiko

CORPORATE SOURCE: Department of Pharmacology, Miyazaki Medical College, Miyazaki, 889-1692, Japan

SOURCE: British Journal of Pharmacology (2000), 130(8), 1727-1730

CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In isolated rat uterine strips, adrenomedullin (AM) inhibited the

spontaneous periodic contraction in a concn.-dependent manner ($IC_{50} = 22.3 \pm 0.7$ nM). The inhibitory effect of AM was prevented by either AM22-52, a putative antagonist for AM receptors, or calcitonin gene-related peptide (CGRP)8-37, a putative antagonist for CGRP receptors. AM also attenuated bradykinin (BK)-induced periodic uterine contraction, which was blocked by AM22-52 or CGRP8-37, whereas AM had no effect on the periodic contraction caused by oxytocin or prostaglandin F2.alpha. (PGF2.alpha.). RT - PCR anal. showed that mRNAs for calcitonin receptor-like receptor (CRLR), receptor-activity-modifying protein (RAMP)1, RAMP2 and RAMP3 were expressed in the rat uterus. These results demonstrate that AM selectively inhibits spontaneous and BK-induced periodic contraction via activating receptors for AM and CGRP.

IT 50-56-6, Oxytocin, biological studies 58-82-2, Bradykinin

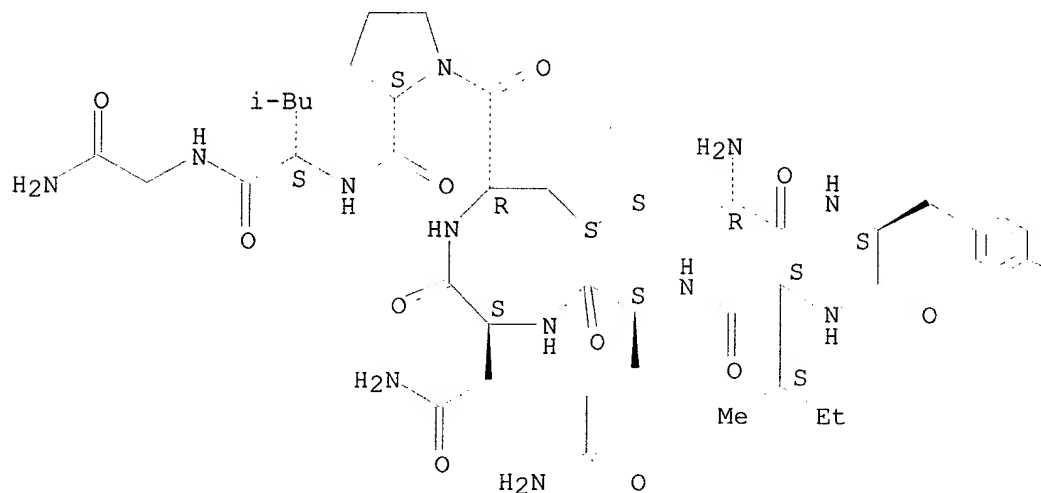
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (adrenomedullin **inhibits** spontaneous and bradykinin-induced but not oxytocin- or prostaglandin F2.alpha.-induced periodic contraction of rat uterus via adrenomedullin **receptors** and **CGRP receptors**)

RN 50-56-6 CAPLUS

CN Oxytocin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

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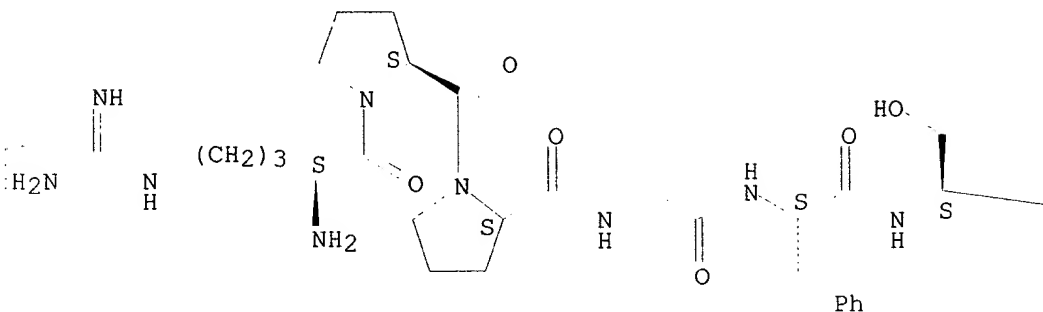
PAGE 1-B

OH

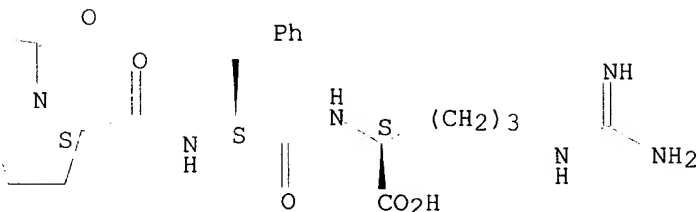
RN 58-82-2 CAPLUS
CN Bradykinin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 9 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:490618 CAPLUS

DOCUMENT NUMBER: 133:188269

TITLE: Characterisation of calcitonin gene
-related peptide receptors

in rat atrium and vas deferens: evidence for a
[Cys(Et)₂,7]hCGRP-preferring receptor

AUTHOR(S): Wu, D.; Eberlein, W.; Rudolf, K.; Engel, W.;
Hallermayer, G.; Doods, H.

CORPORATE SOURCE: Biological and Chemical Research, Boehringer Ingelheim
Pharma KG, Biberach, 88397, Germany

SOURCE: European Journal of Pharmacology (2000), 400(2/3),
313-319

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The present study was performed to characterize calcitonin gene-related
peptide (CGRP) receptor subtypes in rat left atrium and vas deferens by

using [R-(R*,S*)]-N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-4-(1,4-dihydro-2-oxo-3(2H)-quinazolinyl)-,1-Piperidinecarboxamide (BIBN4096BS), a novel CGRP receptor antagonist. When CGRP was used as an agonist, BIBN4096BS exhibited an almost 10-fold higher affinity for CGRP receptors in rat left atrium compared to those in the vas deferens, indicating that CGRP acts through different CGRP receptor subtypes in these two tissues. In addn., BIBN4096BS was almost 10-fold more potent in antagonizing [Cys(Et)2,7]hCGRP.alpha. and human adrenomedullin-induced responses than CGRP-induced responses in rat vas deferens. This might indicate receptor heterogeneity in rat vas deferens. Accordingly, the present work provides first exptl. evidence that the rat vas deferens contains two CGRP-like receptor subtypes. Namely, the CGRP2 receptor and a "novel" receptor that possesses low efficacy for CGRP and that is selectively stimulated by [Cys(Et)2,7]hCGRP or adrenomedullin and which can be blocked with high affinity by BIBN4096BS.

IT 119911-68-1, Human .alpha.-calcitonin gene-

related peptide(8-37) 159435-61-7,
8-37-.beta.-Calcitonin gene-related
peptide (human)

RL: BAC (Biological activity or effector, except adverse); BPR
(Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)

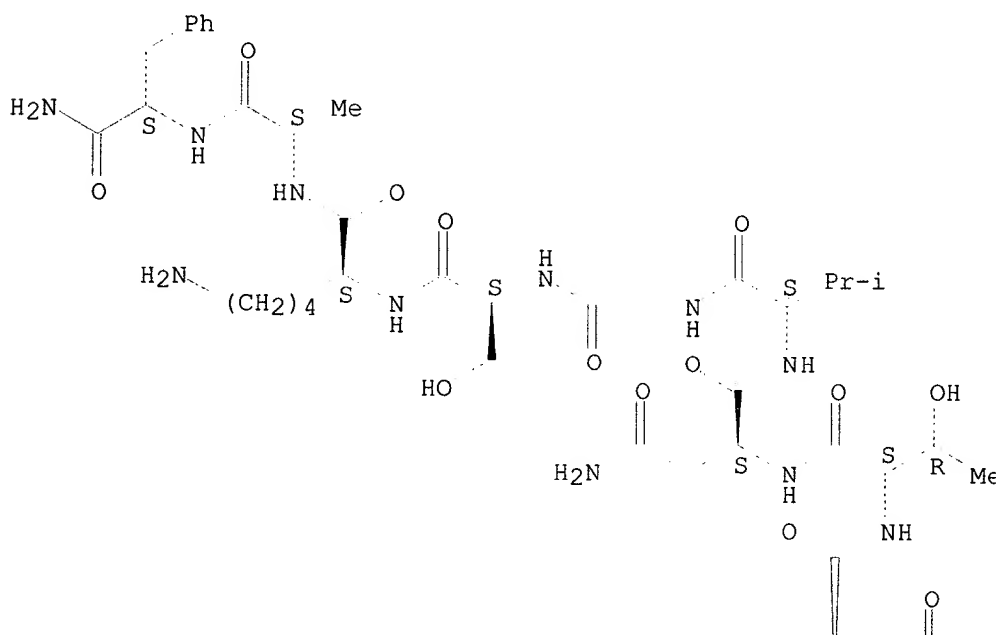
(evidence for CGRP2 and [Cys(Et)2,7]hCGRP or adrenomedullin-preferring
receptor which is blocked with high affinity by BIBN4096BS in
rat atrium and vas deferens)

RN 119911-68-1 CAPLUS

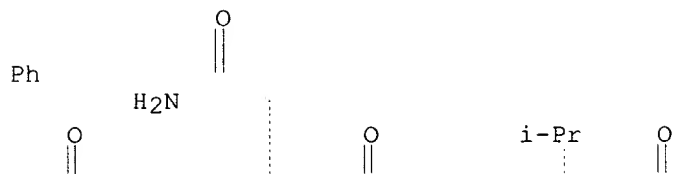
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

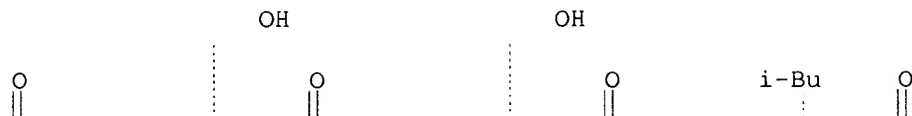
PAGE 1-A



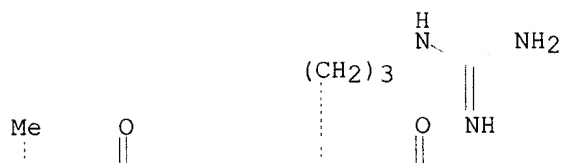
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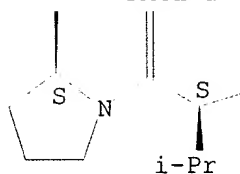
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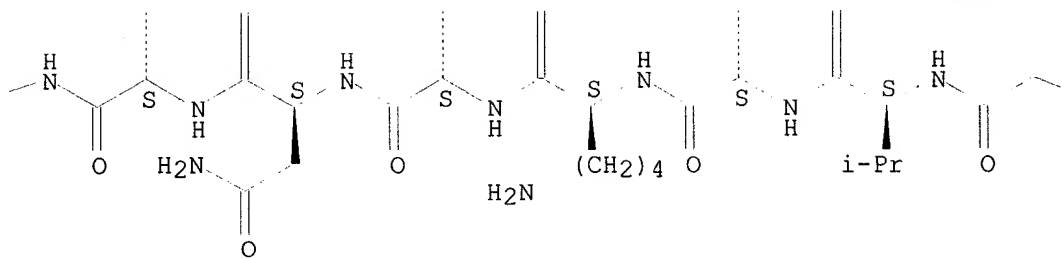
PAGE 1-D



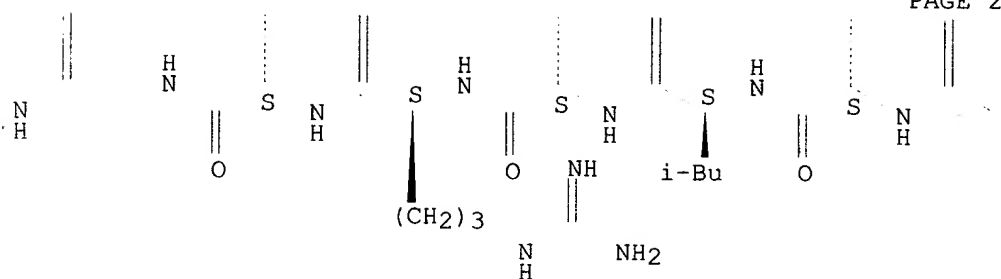
PAGE 2-A



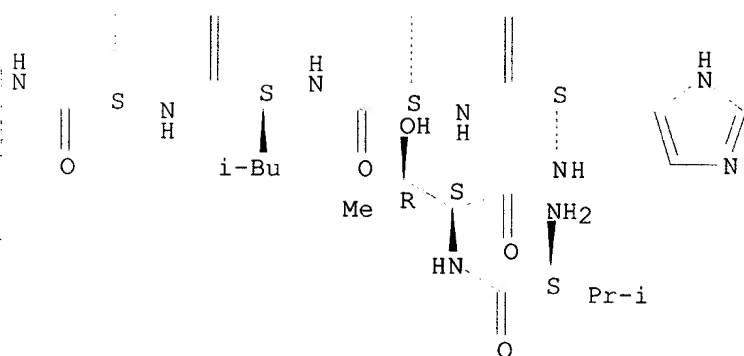
PAGE 2-B



PAGE 2-C



PAGE 2-D

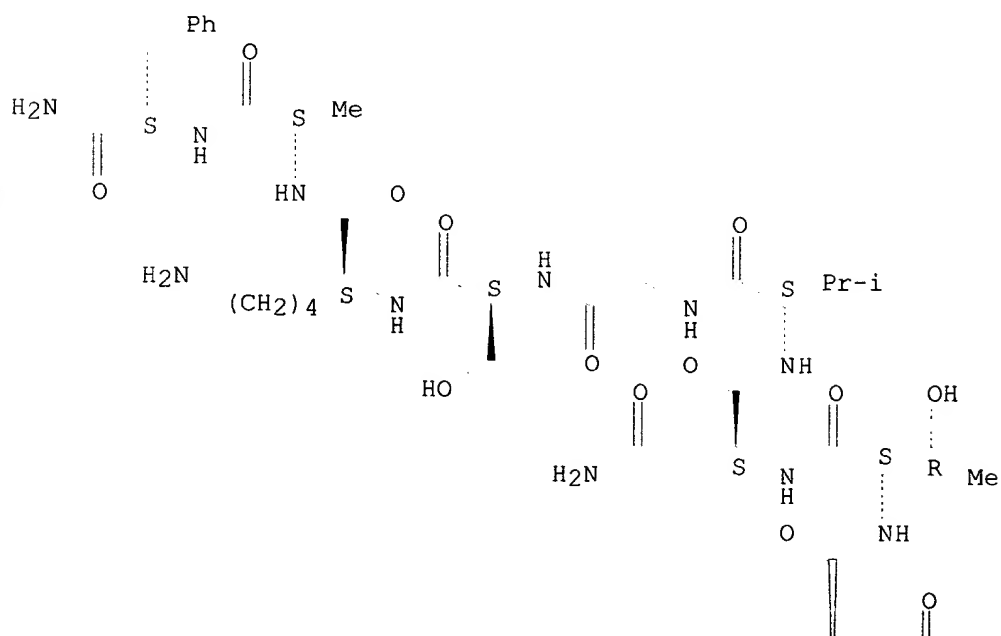


RN 159435-61-7 CAPLUS

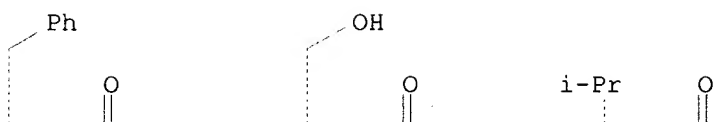
CN 8-37-.beta.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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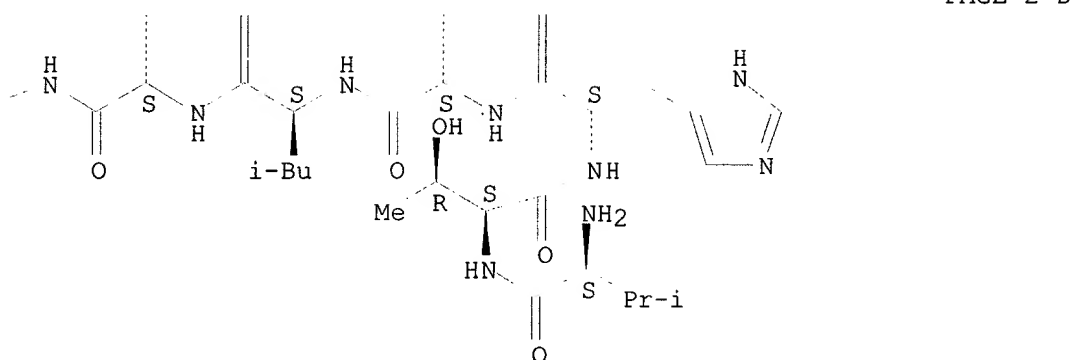
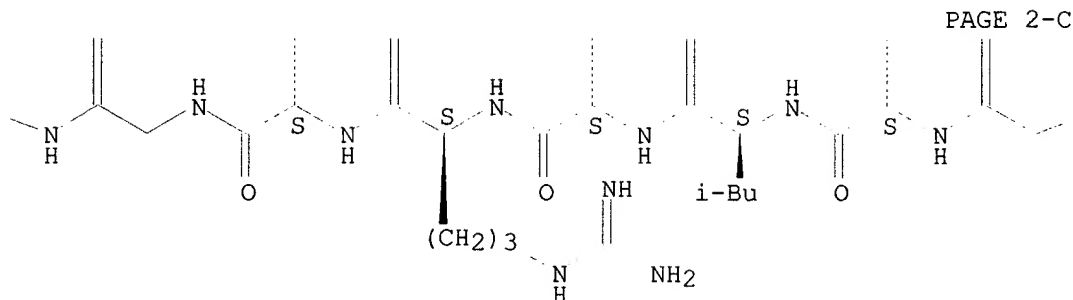
PAGE 1-C



$$\begin{array}{c} \text{H} \\ | \\ (\text{CH}_2)_3 - \text{N} - \text{NH}_2 \\ | \\ \text{O} \\ || \\ \text{NH} \end{array}$$

PAGE 2

Glycyl-L-histidyl-L-histidine
Glycyl-L-histidyl-L-histidyl-L-histidine
Glycyl-L-histidyl-L-histidyl-L-histidyl-L-histidine
Glycyl-L-histidyl-L-histidyl-L-histidyl-L-histidyl-L-histidine
Glycyl-L-histidyl-L-histidyl-L-histidyl-L-histidyl-L-histidyl-L-histidine



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 10 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:277840 CAPLUS

DOCUMENT NUMBER: 132:313697

TITLE: Irrigation solution for inhibition of pain and inflammation

INVENTOR(S): Demopoulos, Gregory A.; Palmer, Pamela P.; Herz, Jeffrey M.

PATENT ASSIGNEE(S): Omeros Medical Systems, Inc., USA

SOURCE: PCT Int. Appl., 115 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023062	A2	20000427	WO 1999-US24558	19991020
WO 2000023062	A3	20000727		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002028798 A1 20020307
PRIORITY APPLN. INFO.:

US 2001-839633 20010420
US 1998-105044P P 19981020
US 1994-353775 B2 19941212
WO 1995-US16028 A2 19951212
US 1996-670699 A2 19960626
US 1998-72913 A2 19980504
US 1998-105026P P 19981020
US 1998-105029P P 19981020
US 1998-105166P P 19981021
US 1998-107256P P 19981105
WO 1999-US24557 A2 19991020
WO 1999-US24558 A2 19991020
WO 1999-US24625 A2 19991020
WO 1999-US24672 A2 19991020
WO 1999-US26330 A2 19991105

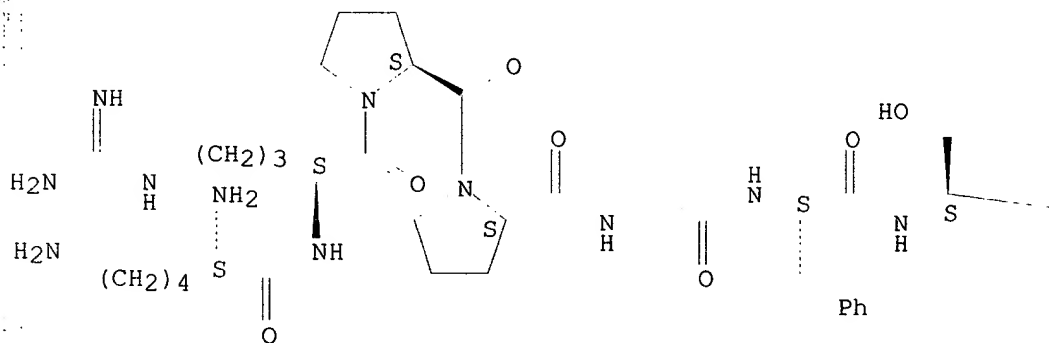
AB A method and soln. for perioperatively inhibiting a variety of pain and inflammation processes at wounds from general surgical procedures including oral/dental procedures. The soln. preferably includes at least 1 neuronal nicotinic acetylcholine receptor agonist and, optionally, addnl. multiple pain and inflammation inhibitory agents at dil. concn. in a physiol. carrier, such as saline or lactated Ringer's soln. The soln. is applied by continuous irrigation of a wound during a surgical procedure for preemptive inhibition of pain and while avoiding undesirable side effects assocd. with oral, i.m., s.c. or i.v. application of larger doses of the agents. One preferred soln. to inhibit pain and inflammation includes a neuronal nicotinic acetylcholine receptor agonist, serotonin receptor-2 and serotonin receptor-3 antagonists, a histamine antagonist, a serotonin agonist, a cyclooxygenase inhibitor, neurokinin receptor-1 and neurokinin receptor-2 antagonists, a purinoceptor antagonist, an ATP-sensitive potassium channel opener, calcium channel, bradykinin receptor-1 and bradykinin receptor-2 antagonists, and a .mu.-opioid agonist. Thus, an irrigation soln. for cardiovascular and general vascular therapeutic and diagnostic procedures consists of a serotonin receptor-2 antagonist, LY-53857 50 nM.

IT 71800-37-8 128270-60-0, Hirulog 129623-01-4,
GR 82334 138614-30-9, HOE 140 138680-92-9
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(irrigation soln. for inhibition of pain and inflammation)

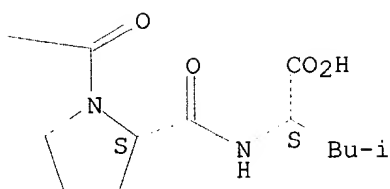
RN 71800-37-8 CAPLUS
CN 1-9-Kallidin, 9-L-leucine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

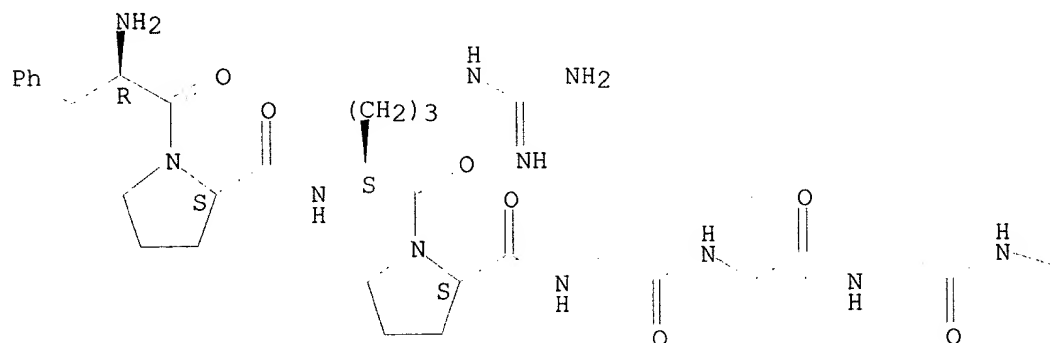


RN 128270-60-0 CAPLUS

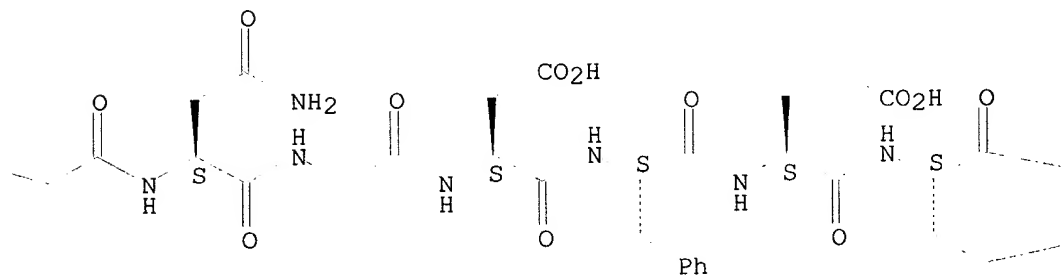
CN L-Leucine, D-phenylalanyl-L-prolyl-L-arginyl-L-prolylglycylglycylglycylglycyl-L-asparaginylglycyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-isoleucyl-L-prolyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

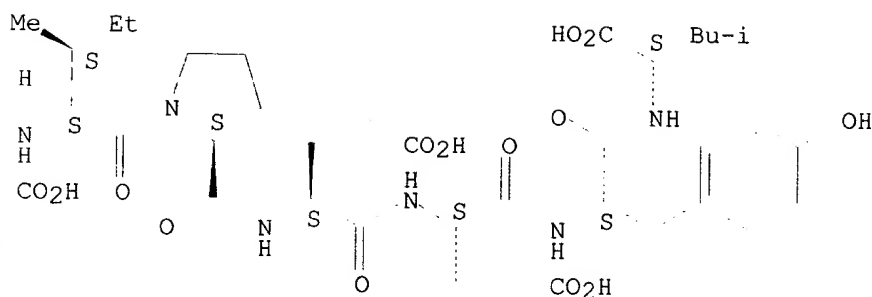
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PAGE 1-B



PAGE 1-C

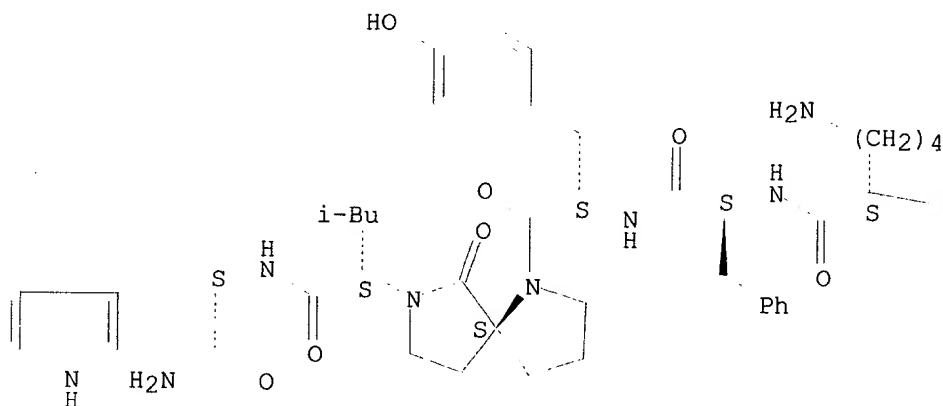


RN 129623-01-4 CAPLUS

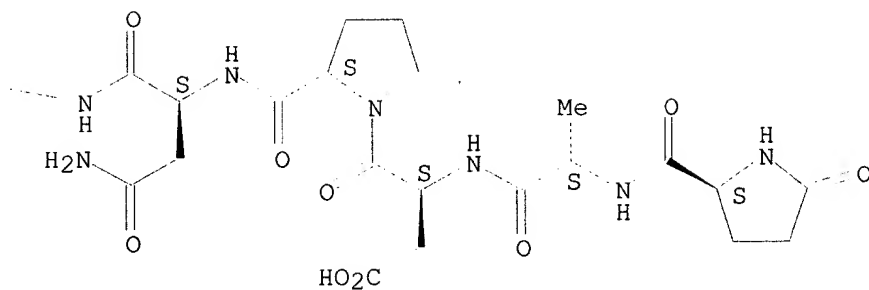
CN L-Tryptophanamide, 5-oxo-L-prolyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-lysyl-L-phenylalanyl-L-tyrosyl-(.alpha.S,5S)-.alpha.-(2-methylpropyl)-6-oxo-1,7-diazaspiro[4.4]nonane-7-acetyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



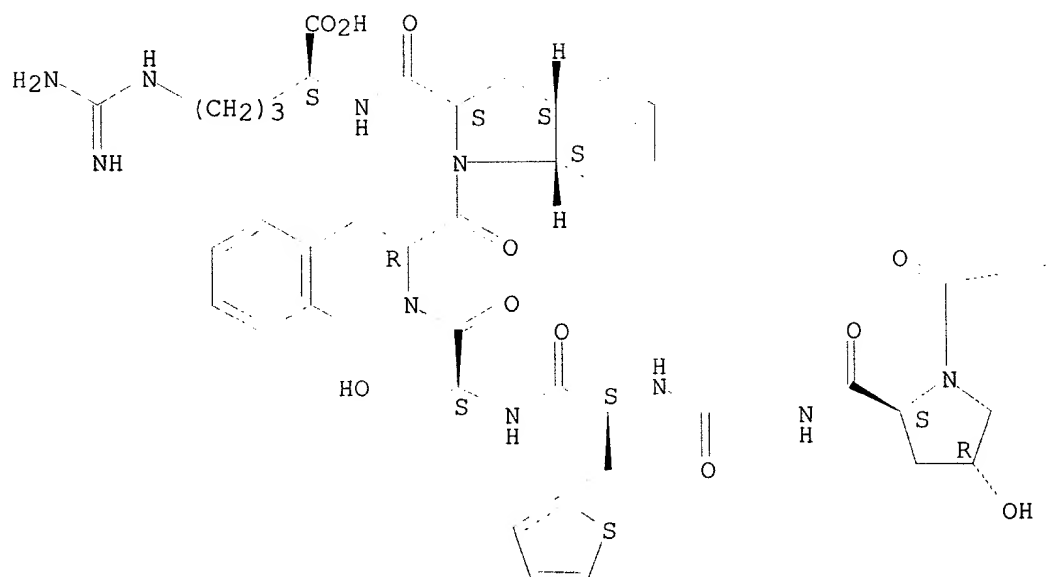
RN 138614-30-9 CAPLUS
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CM 1

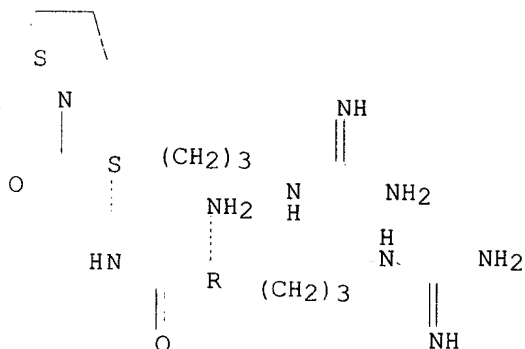
CRN 130308-48-4
 CMF C59 H89 N19 O13 S
 CDES *

Absolute stereochemistry.

PAGE 1-A



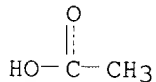
PAGE 1-B



CM 2

CRN 64-19-7

CMF C2 H4 O2

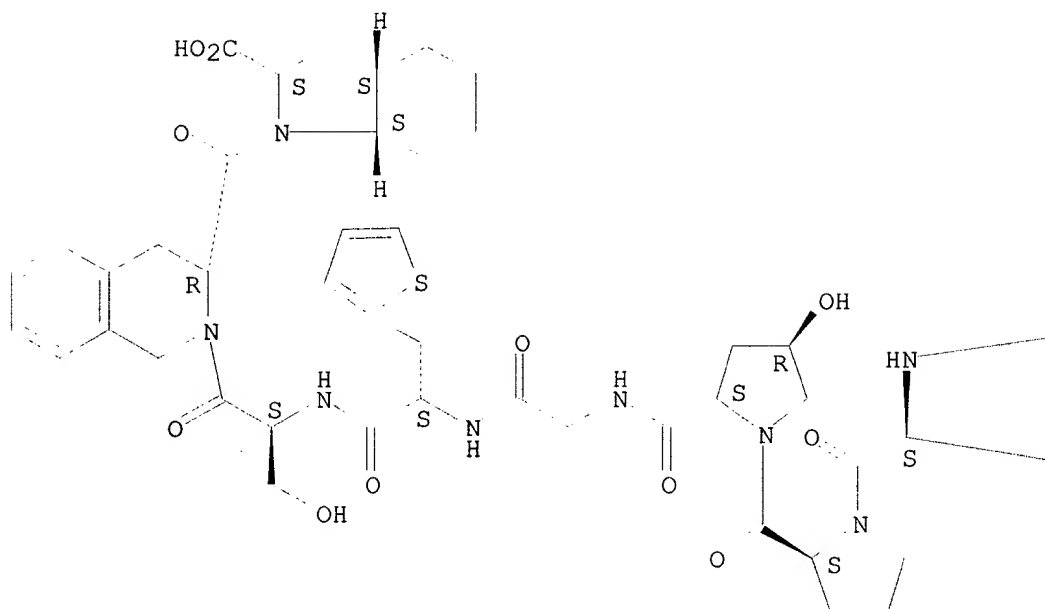


RN 138680-92-9 CAPLUS

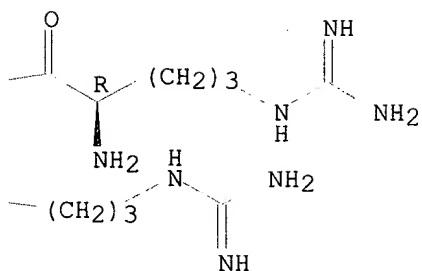
CN 1H-Indole-2-carboxylic acid, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyloctahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L25 ANSWER 11 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:277839 CAPLUS

DOCUMENT NUMBER: 132:313696

TITLE: Irrigation solution and method for inhibition of pain and inflammation

INVENTOR(S): Demopoulos, Gregory A.; Palmer, Pamela P.; Herz, Jeffrey M.

PATENT ASSIGNEE(S): Omeros Medical Systems, Inc., USA

SOURCE: PCT Int. Appl., 114 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

Searched by Barb O'Bryen, STIC 308-4291

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000023061	A2	20000427	WO 1999-US24557	19991020
WO 2000023061	A3	20001116		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002028798	A1	20020307	US 2001-839633	20010420
PRIORITY APPLN. INFO.:				
			US 1998-105166P	P 19981021
			US 1994-353775	B2 19941212
			WO 1995-US16028	A2 19951212
			US 1996-670699	A2 19960626
			US 1998-72913	A2 19980504
			US 1998-105026P	P 19981020
			US 1998-105029P	P 19981020
			US 1998-105044P	P 19981020
			US 1998-107256P	P 19981105
			WO 1999-US24557	A2 19991020
			WO 1999-US24558	A2 19991020
			WO 1999-US24625	A2 19991020
			WO 1999-US24672	A2 19991020
			WO 1999-US26330	A2 19991105

AB A method and soln. for perioperatively inhibiting a variety of pain and inflammation processes at wounds from general surgical procedures including oral/dental procedures. The soln. preferably includes at least 1 neuronal nicotinic acetylcholine receptor agonist and, optionally, addnl. multiple pain and inflammation inhibitory agents at dil. concn. in a physiol. carrier, such as saline or lactated Ringer's soln. The soln. is applied by continuous irrigation of a wound during a surgical procedure for preemptive inhibition of pain and while avoiding undesirable side effects assocd. with oral, i.m., s.c. or i.v. application of larger doses of the agents. One preferred soln. to inhibit pain and inflammation includes a neuronal nicotinic acetylcholine receptor agonist, serotonin receptor-2 and serotonin receptor-3 antagonists, a histamine antagonist, a serotonin agonist, a cyclooxygenase inhibitor, neurokinin receptor-1 and neurokinin receptor-2 antagonists, a purinoceptor antagonist, an ATP-sensitive potassium channel opener, calcium channel, bradykinin receptor-1 and bradykinin receptor-2 antagonists, and a .mu.-opioid agonist. Thus, an irrigation soln. for cardiovascular and general vascular therapeutic and diagnostic procedures consists of a serotonin receptor-2 antagonist, LY-53857 50 nM.

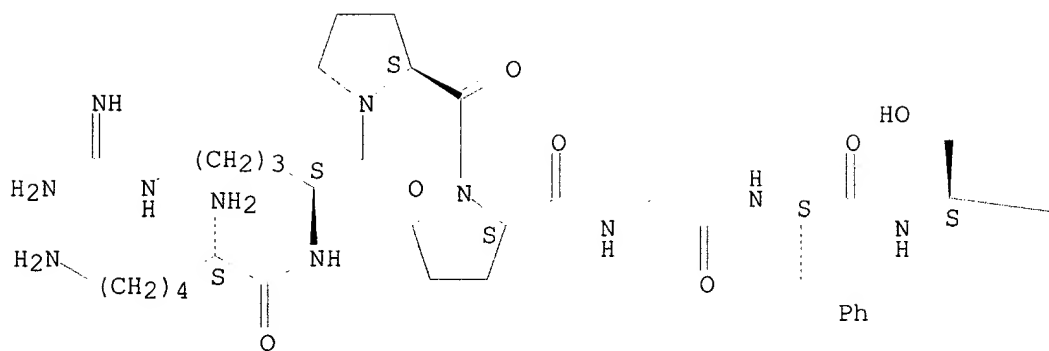
IT 71800-37-8 128270-60-0, Hirulog 129623-01-4,
GR 82334 138614-30-9, HOE 140 138680-92-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation soln. for inhibition of pain and inflammation)

RN 71800-37-8 CAPLUS

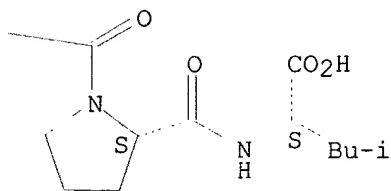
CN 1-9-Kallidin, 9-L-leucine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

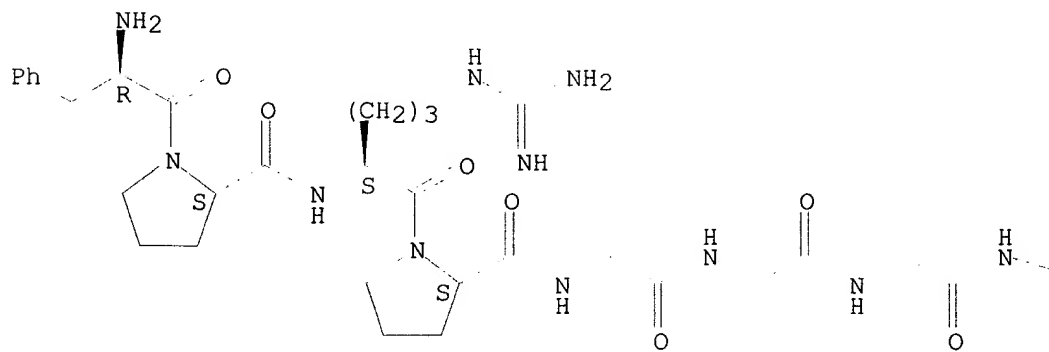


RN 128270-60-0 CAPLUS

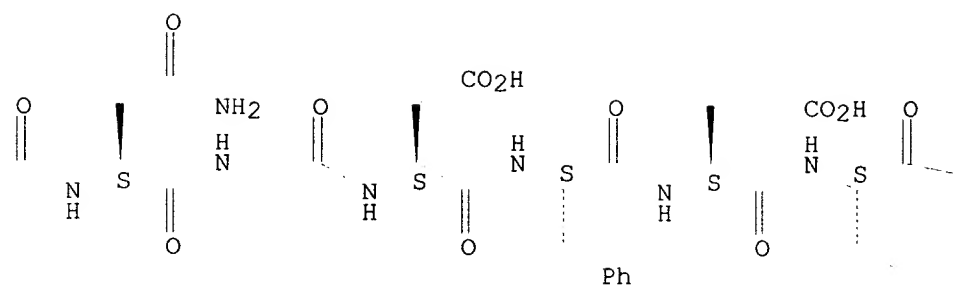
CN L-Leucine, D-phenylalanyl-L-prolyl-L-arginyl-L-prolylglycylglycylglycylglycyl-L-asparaginyglycyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-isoleucyl-L-prolyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

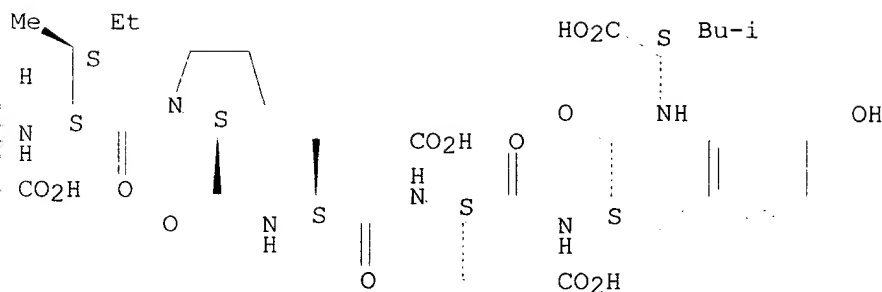
PAGE 1-A



PAGE 1-B



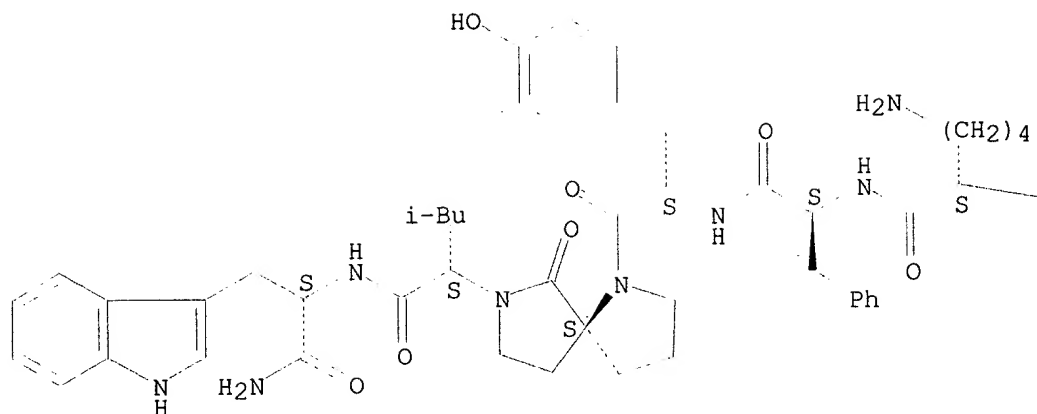
PAGE 1-C



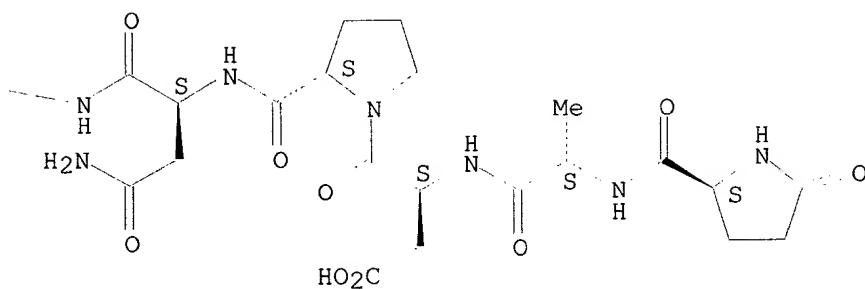
RN 129623-01-4 CAPLUS
 CN L-Tryptophanamide, 5-oxo-L-prolyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-lysyl-L-phenylalanyl-L-tyrosyl-(.alpha.S,5S)-.alpha.-(2-methylpropyl)-6-oxo-1,7-diazaspiro[4.4]nonane-7-acetyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



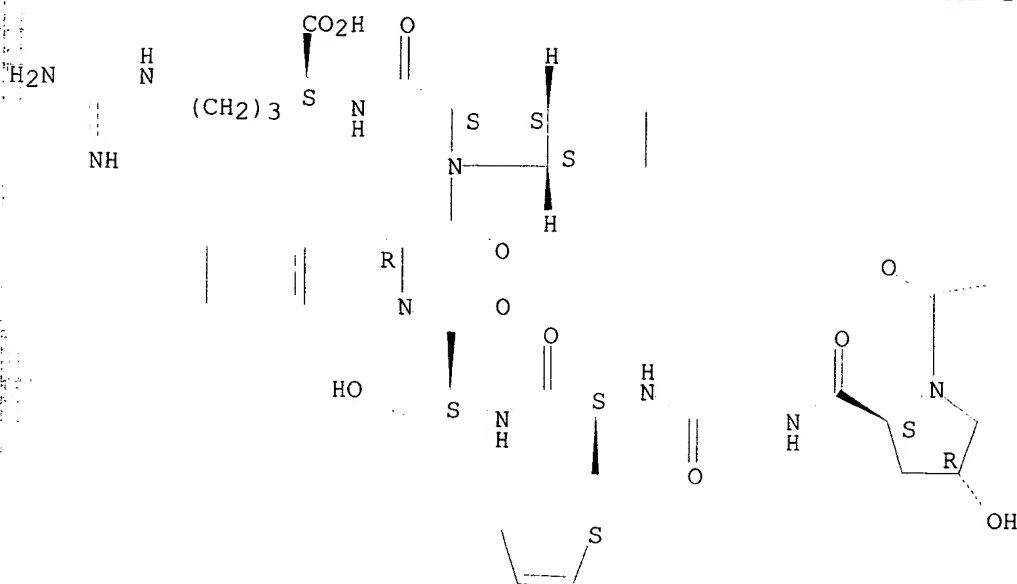
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CM 1

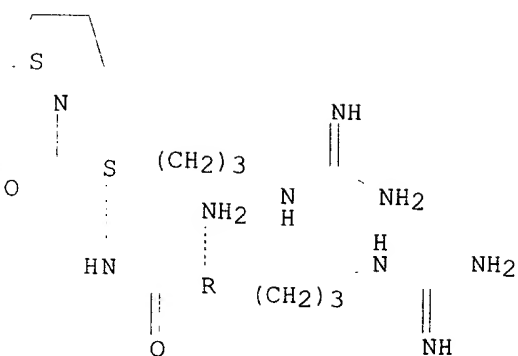
CRN 130308-48-4
 CMF C59 H89 N19 O13 S
 CDES *

Absolute stereochemistry.

PAGE 1-A

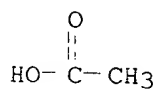


PAGE 1-B



CM 2

CRN 64-19-7
 CMF C2 H4 O2

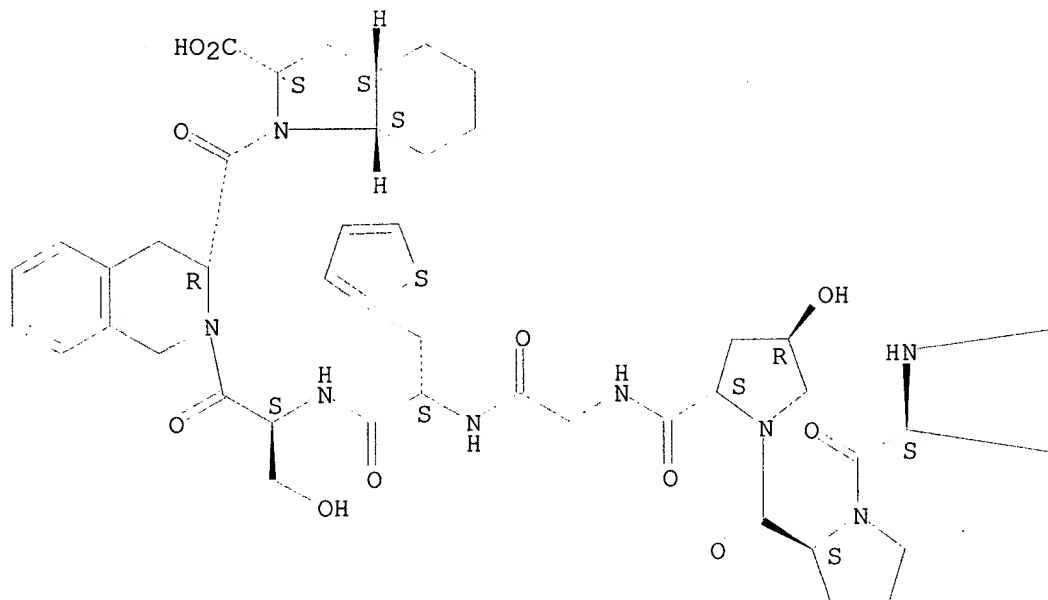


RN 138680-92-9 CAPLUS

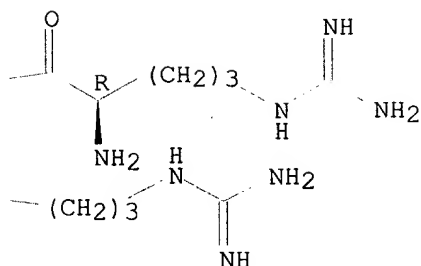
CN 1H-Indole-2-carboxylic acid, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyloctahydro-, (2S,3aS,7aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L25 ANSWER 12 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:183622 CAPLUS

DOCUMENT NUMBER: 132:318115

TITLE: Bioactive .beta.-bend structures for the antagonist h.alpha. CGRP8-37 at the CGRP1 receptor of the rat

Searched by Barb O'Bryen, STIC 308-4291

AUTHOR(S): pulmonary artery
Wisskirchen, F. M.; Doyle, P. M.; Gough, S. L.;
Harris, C. J.; Marshall, I.
CORPORATE SOURCE: Department of Pharmacology, University College London,
London, WC1E 6BT, UK
SOURCE: British Journal of Pharmacology (2000), 129(5),
1049-1055
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1 The aim of this study was to det. .beta.-bend structures and the role of the N- and C-terminus in the antagonist h.alpha. CGRP8-37 at the rat pulmonary artery CGRP receptor mediating h.alpha. CGRP relaxation. 2 H.alpha. CGRP8-37 Pro16 (10-6 M), with a bend-biasing residue (proline) at position 16, did not antagonize h.alpha. CGRP responses, while a structure-conserving amino acid (alanine16) at the same position retained antagonist activity (apparent pKB 6.6.+-.0.1; 10-6 M). H.alpha. CGRP8-37 Pro19 (10-6 M), with proline at position 19 was an antagonist (apparent pKB 6.9.+-.0.1). 3 Incorporation of a .beta.-bend forcing residue, BTD (beta-turn dipeptide), at positions 19 and 20 in h.alpha. CGRP8-37 (10-6 M) antagonized h.alpha. CGRP responses (apparent pKB 7.2.+-.0.2); and BTD at positions 19,20 and 33,34 within h.alpha. CGRP8-37 was a competitive antagonist (pA2 7.2; Schild plot slope 1.0.+-.0.1). 4 H.alpha. CGRP8-37 analogs, substituted at the N-terminus by either glycine8 or des-NH2 valine8 or proline8 were all antagonists (apparent pKB 6.9.+-.0.1; (10-6 M), 7.0.+-.0.1 (10-6 M), and pA2 7.0 (slope 1.0.+-.0.2), resp.); while replacements by proline8 together with glutamic acid10,14 in h.alpha. CGRP8-37 (10-6 M) or alanine amide37 at the C-terminus of h.alpha. CGRP8-37 (10-5 M) were both inactive compds. 5 In conclusion, possible bioactive structures of h.alpha. CGRP8-37 include two .beta.-bends (at 18-21 and 32-35), which were mimicked by BTD incorporation. Within h.alpha. CGRP8-37, the N-terminus is not essential for antagonism while the C-terminus may interact directly with CGRP1 receptors in the rat pulmonary artery.

IT 119911-68-1, Human .alpha.-Calcitonin gene-related peptide 8-37 119911-68-1D, Human .alpha.-Calcitonin gene-related peptide 8-37, analogs 195832-30-5 226214-38-6 226214-39-7 226214-40-0 226214-44-4 226214-46-6 226214-47-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(bioactive .beta.-bend structures for the antagonist h.alpha.-CGRP8-37 at the CGRP1 receptor of the rat pulmonary artery)

RN 119911-68-1 CAPLUS

CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

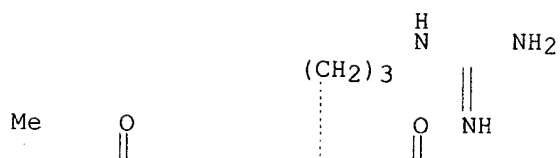
Chemical structures of various thiocarbonyl compounds, including thioamides, thioesters, and thioacetals, with labels like Ph, Me, H₂N, HO, Pr-i, R, and Me.

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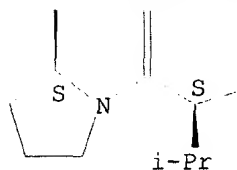
PAGE 1-C



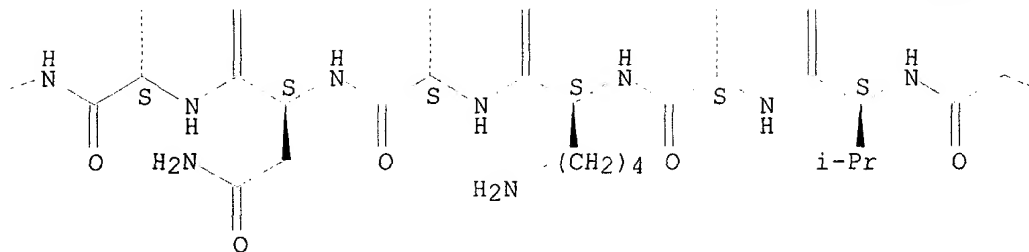
PAGE 1-D



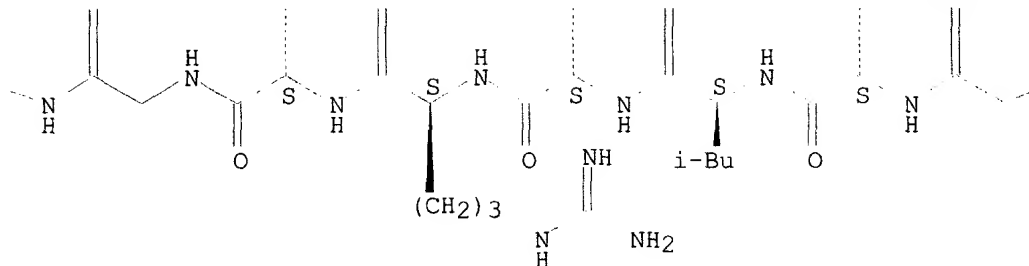
PAGE 2-A



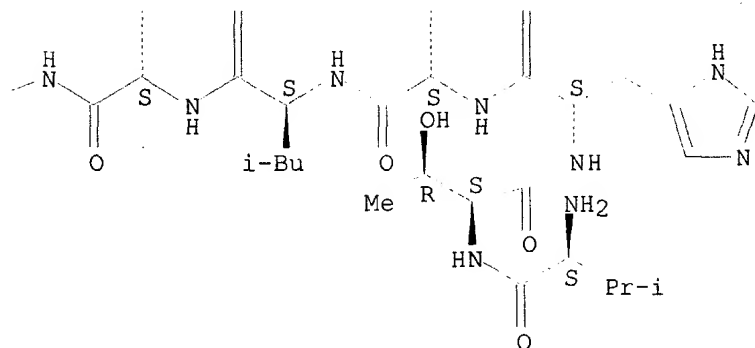
PAGE 2-B



PAGE 2-C



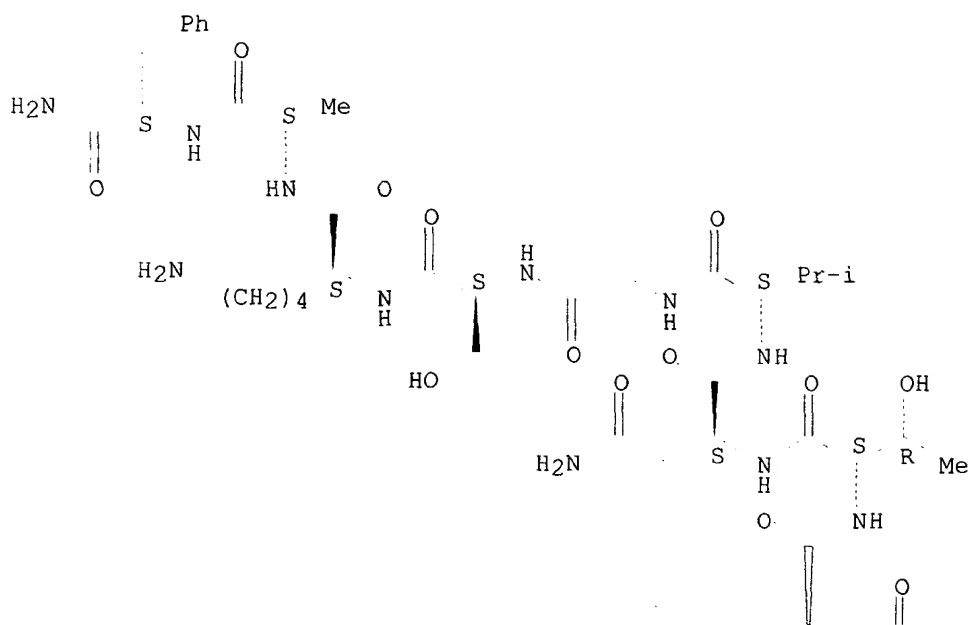
PAGE 2-D



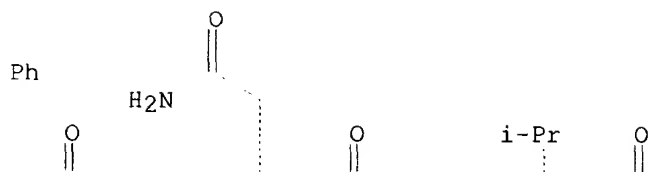
RN 119911-68-1 CAPLUS
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

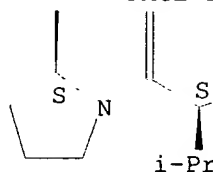


PAGE 1-B

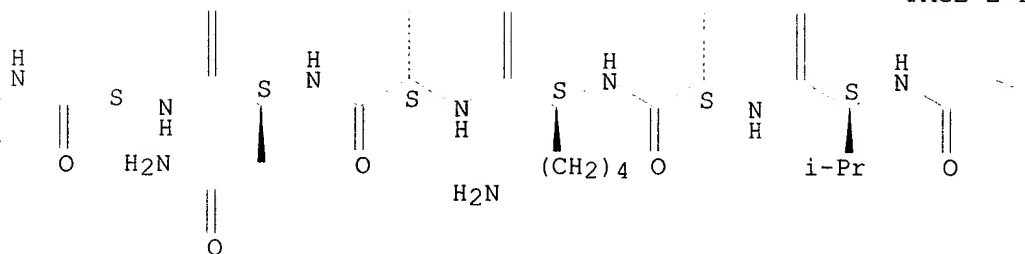


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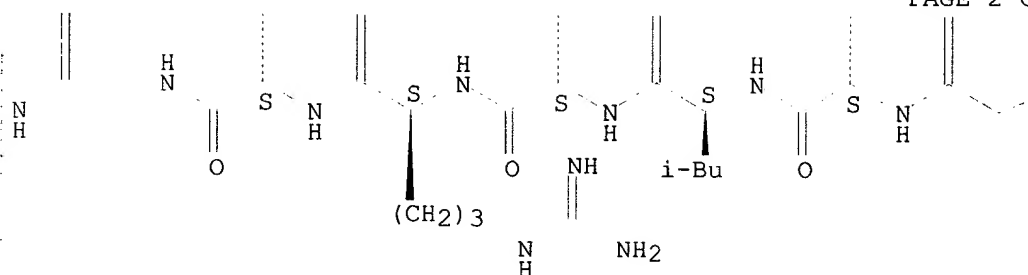
PAGE 2-A



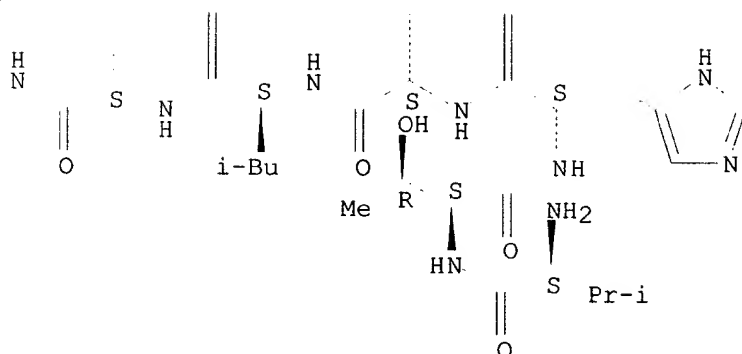
PAGE 2-B



PAGE 2-C



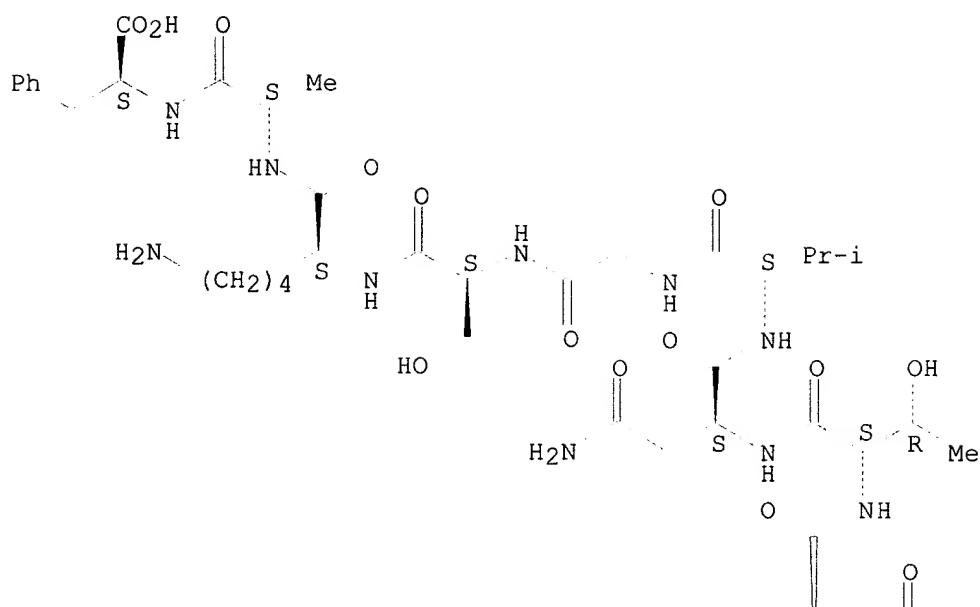
PAGE 2-D



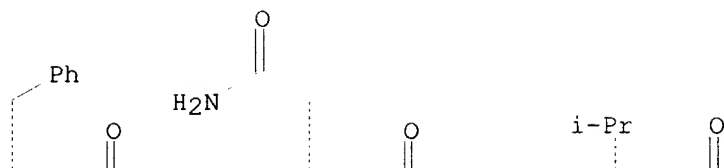
RN 195832-30-5 CAPLUS
 CN 8-37-.alpha.-Calcitonin gene-related peptide (human reduced),
 37-L-phenylalanine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



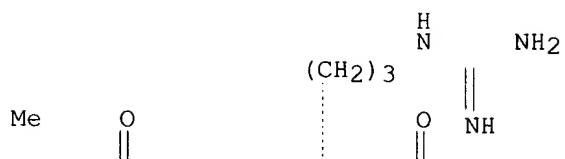
PAGE 1-B



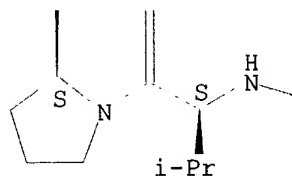
PAGE 1-C



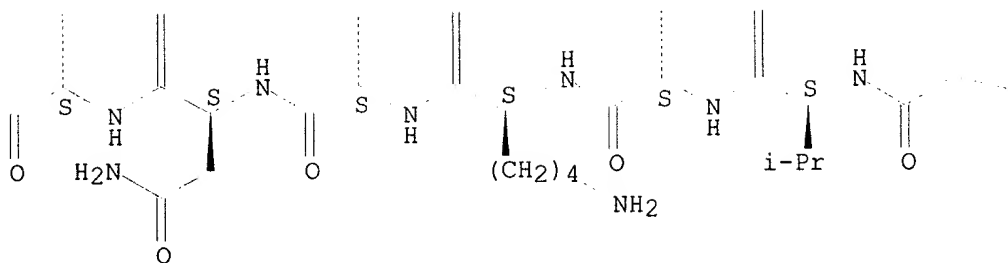
PAGE 1-D



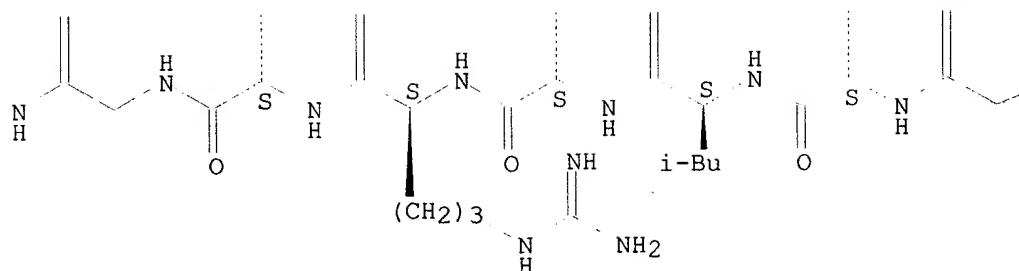
PAGE 2-A



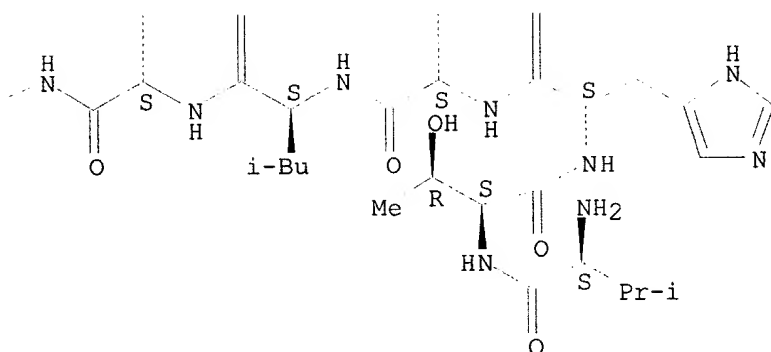
PAGE 2-B



PAGE 2-C



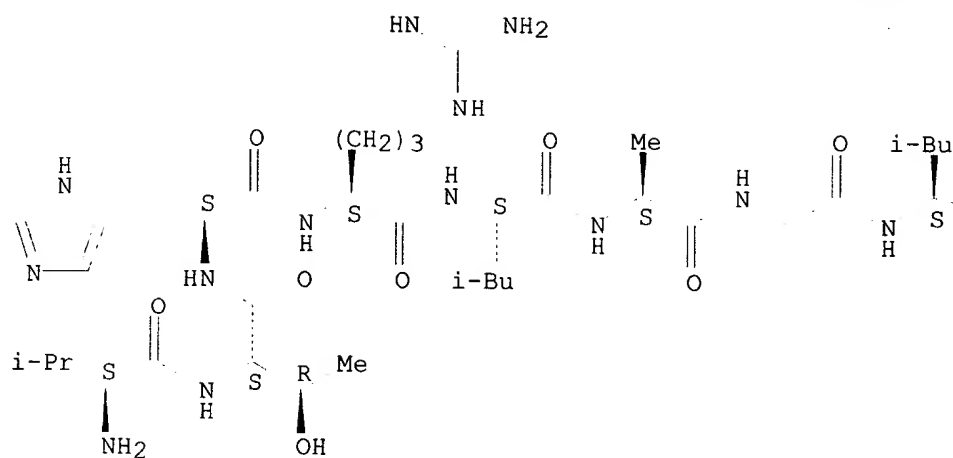
PAGE 2-D



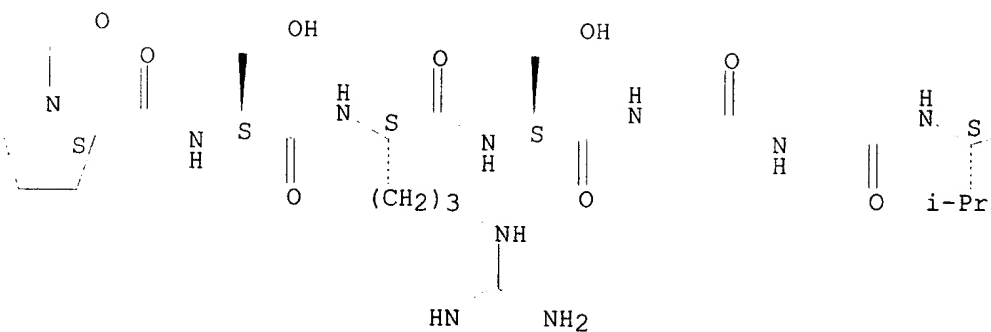
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 CN L-Phenylalaninamide, L-valyl-L-threonyl-L-histidyl-L-arginyl-L-leucyl-L-alanylglycyl-L-leucyl-L-prolyl-L-seryl-L-arginyl-L-serylglycylglycyl-L-valyl-L-valyl-L-lysyl-L-asparaginyl-L-asparaginyl-L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-lysyl-L-alanyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

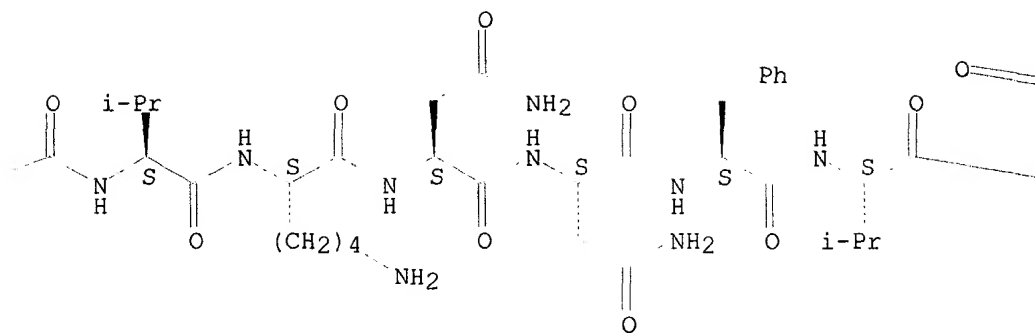
PAGE 1-A



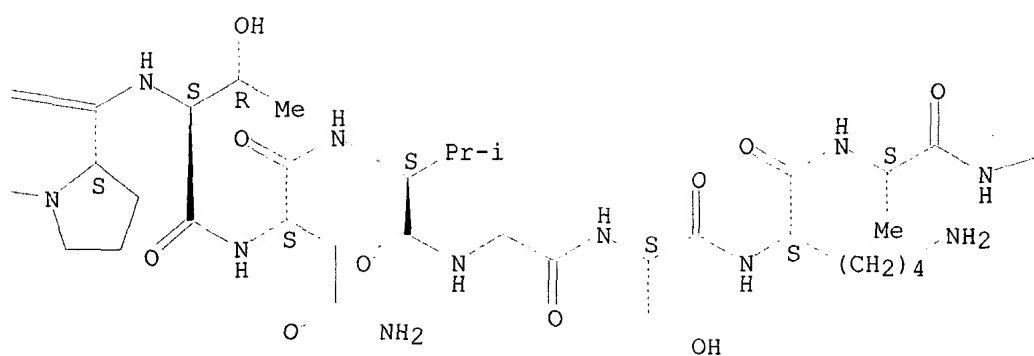
PAGE 1-B



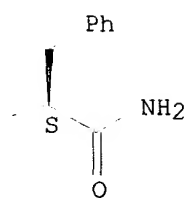
PAGE 1-C



PAGE 1-D



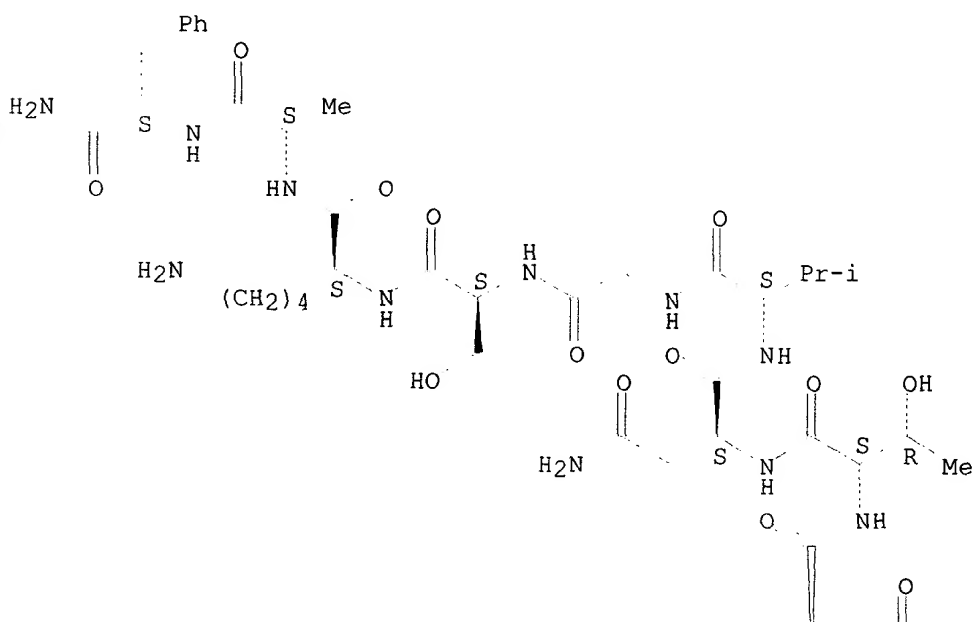
PAGE 1-E



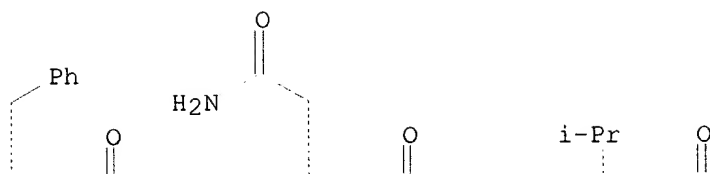
RN 226214-39-7 CAPLUS
CN L-Phenylalaninamide, L-valyl-L-threonyl-L-histidyl-L-arginyl-L-leucyl-L-alanylglycyl-L-leucyl-L-alanyl-L-seryl-L-arginyl-L-serylglycylglycyl-L-valyl-L-valyl-L-lysyl-L-asparaginyl-L-asparaginyl-L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-lysyl-L-alanyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 1-C



$$\text{Me} \quad \text{O} \quad \text{H} \quad \text{NH}_2$$

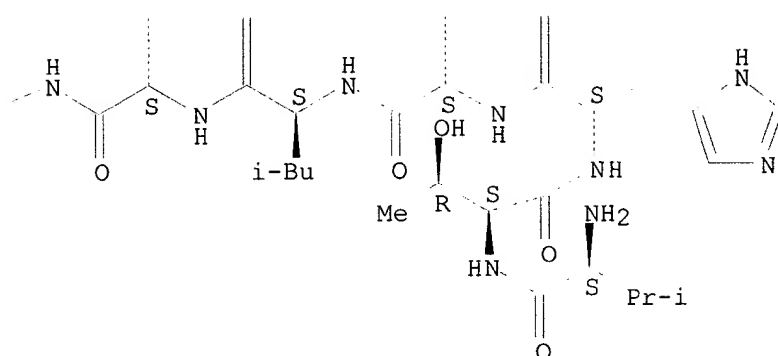
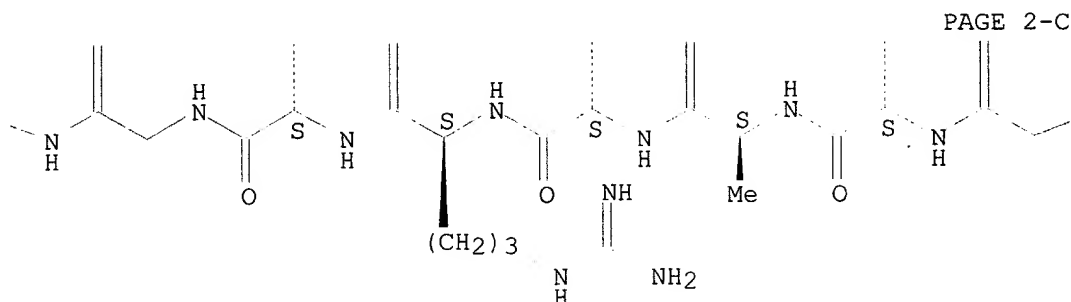
$$\parallel \quad \text{---} \quad \text{N} \quad \parallel$$

$$\text{---} \quad \text{O} \quad \text{NH}$$

$$\text{---} \quad \text{---} \quad \text{---}$$

The image shows two chemical structures. The left structure is 2-methyl-2-thiazolidine, a five-membered ring with a sulfur atom (S) and a nitrogen atom (N), and a methyl group attached to the carbon between them. The right structure is 2-methyl-2-isopropylthiazolidine, which is similar but has an isopropyl group (labeled i-Pr) attached to the carbon between the sulfur and nitrogen atoms.

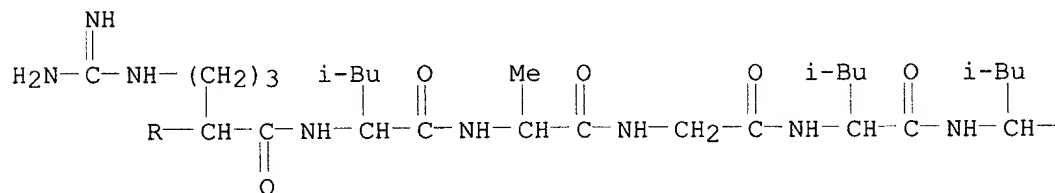
Chemical structures of the polymers are shown in Figure 1. The polymers were prepared by the reaction of the corresponding diisocyanate with the diamine in the presence of a catalyst. The polymers were characterized by infrared and ¹H NMR spectroscopy. The infrared spectra showed the characteristic absorption bands of the urethane and amide groups. The ¹H NMR spectra showed the characteristic peaks of the polymers. The polymers were characterized by their inherent viscosity and glass transition temperature (T_g). The inherent viscosity of the polymers was measured in dimethyl sulfoxide (DMSO) at 30°C. The T_g of the polymers was determined by differential scanning calorimetry (DSC).



RN 226214-40-0 CAPLUS

CN L-Phenylalaninamide, L-valyl-L-threonyl-L-histidyl-L-arginyl-L-leucyl-L-alanylglycyl-L-leucyl-L-leucyl-L-seryl-L-arginyl-L-prolylglycylglycyl-L-valyl-L-valyl-L-lysyl-L-asparaginyl-L-asparaginyl-L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-lysyl-L-alanyl-(9CI) (CA INDEX NAME)

PAGE 1-A

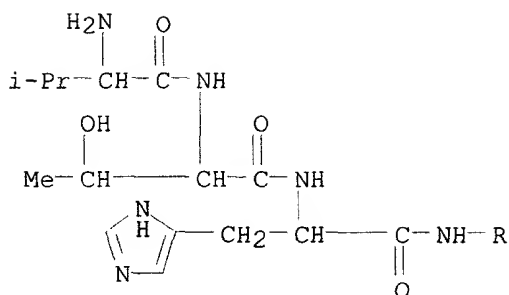


$$\begin{array}{c} \text{O} & \text{HO-CH}_2 & (\text{CH}_2)_3\text{-NH-C(=NH)-NH}_2 \\ || & | & | \\ -\text{C}-\text{NH}-\text{CH}-\text{C}(=\text{O})-\text{NH}-\text{CH} \\ & || & || \\ & \text{O} & \text{N} \\ & & \text{C(=O)-NH-CH}_2\text{-C(=O)-NH-CH}_2\text{-C(=O)-NH-CH(i-Pr)-C(=O)-NH-CH(i-Pr)-} \end{array}$$
[illegible][illegible]

PAGE 1-E

—NH₂

PAGE 2-A

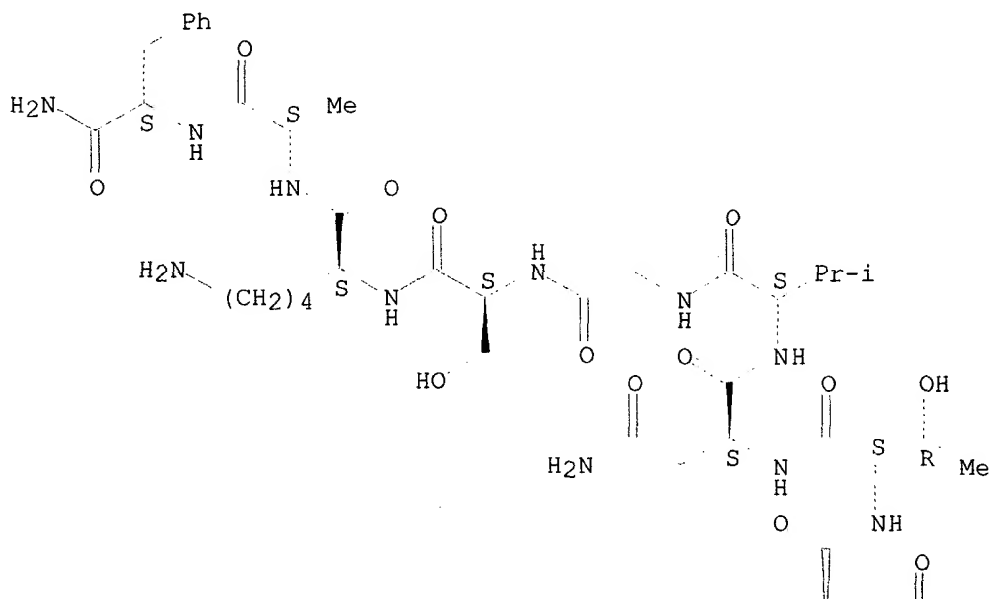


RN 226214-44-4 CAPLUS

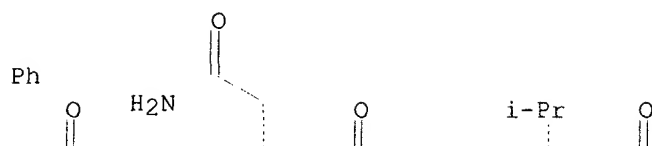
CN L-Phenylalaninamide, glycyl-L-threonyl-L-histidyl-L-arginyl-L-leucyl-L-alanylglycyl-L-leucyl-L-leucyl-L-seryl-L-arginyl-L-serylglycylglycyl-L-valyl-L-valyl-L-lysyl-L-asparaginyl-L-asparaginyl-L-phenylalanyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-lysyl-L-alanyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



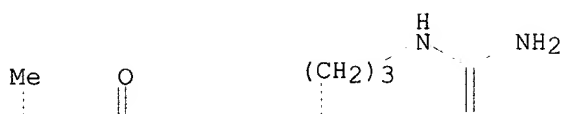
PAGE 1-B



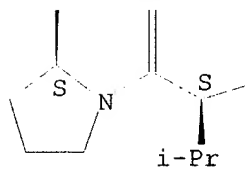
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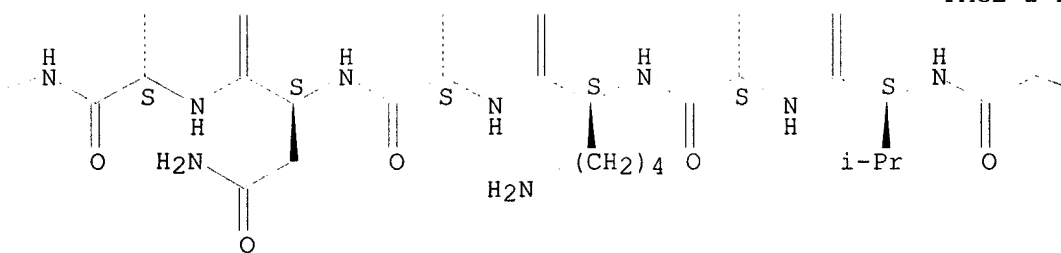
PAGE 1-D



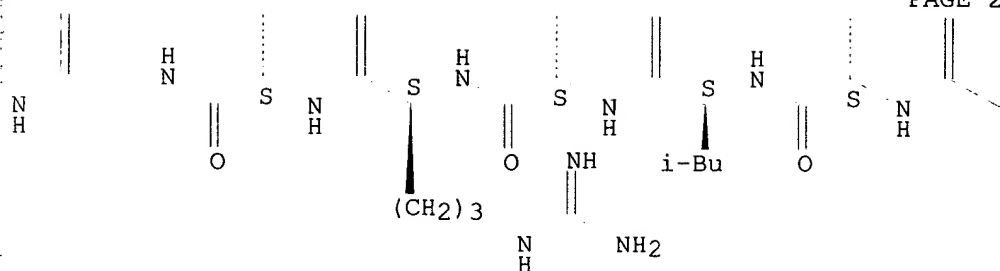
PAGE 2-A



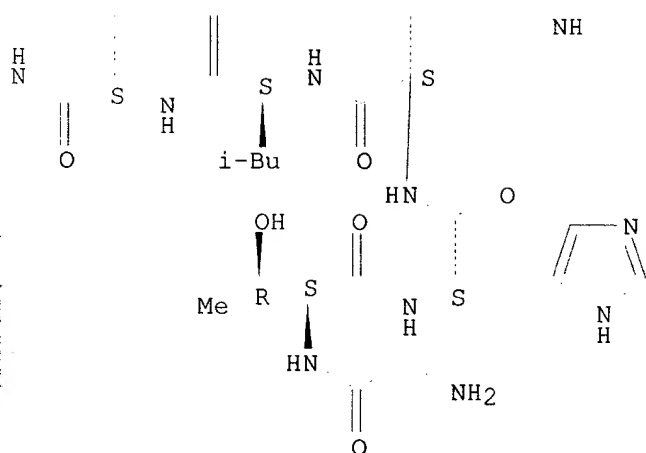
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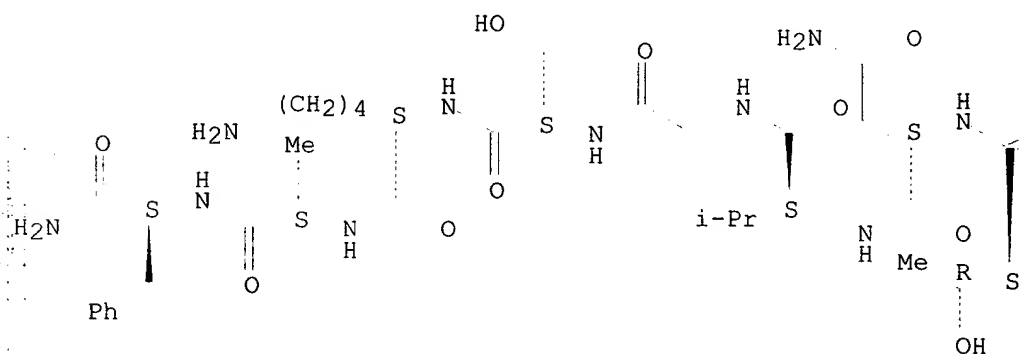
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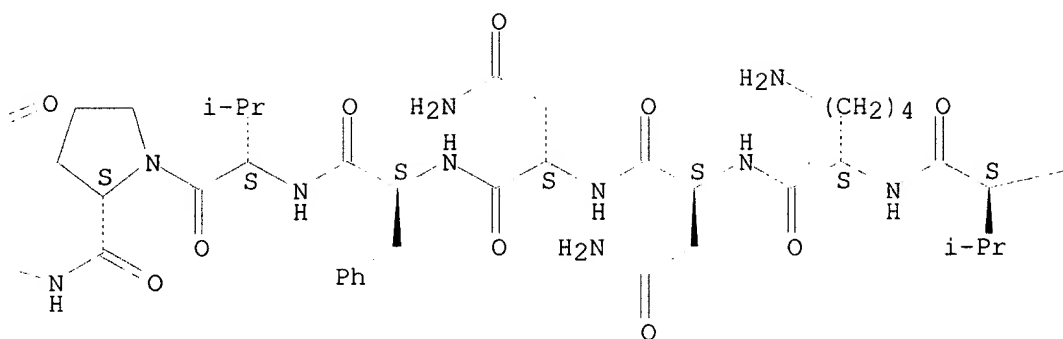
RN 226214-46-6 CAPLUS
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Absolute stereochemistry.

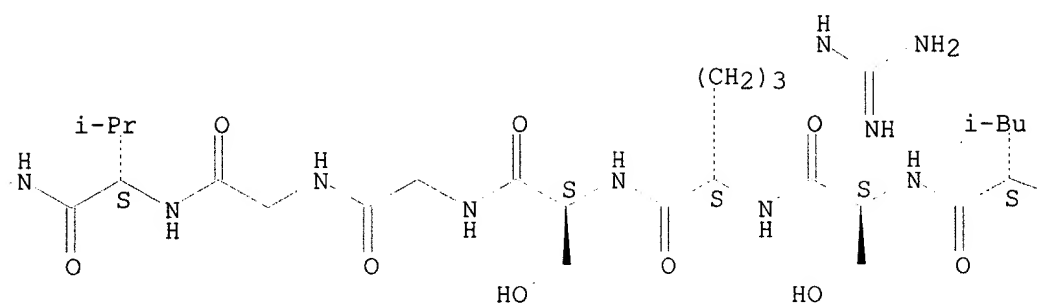
PAGE 1-A



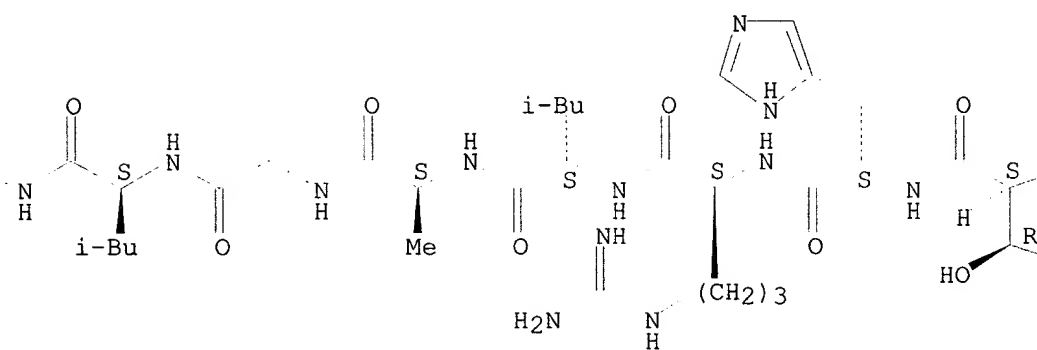
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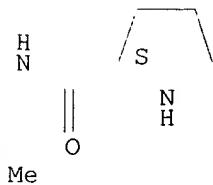
PAGE 1-C



PAGE 1-D



PAGE 1-E

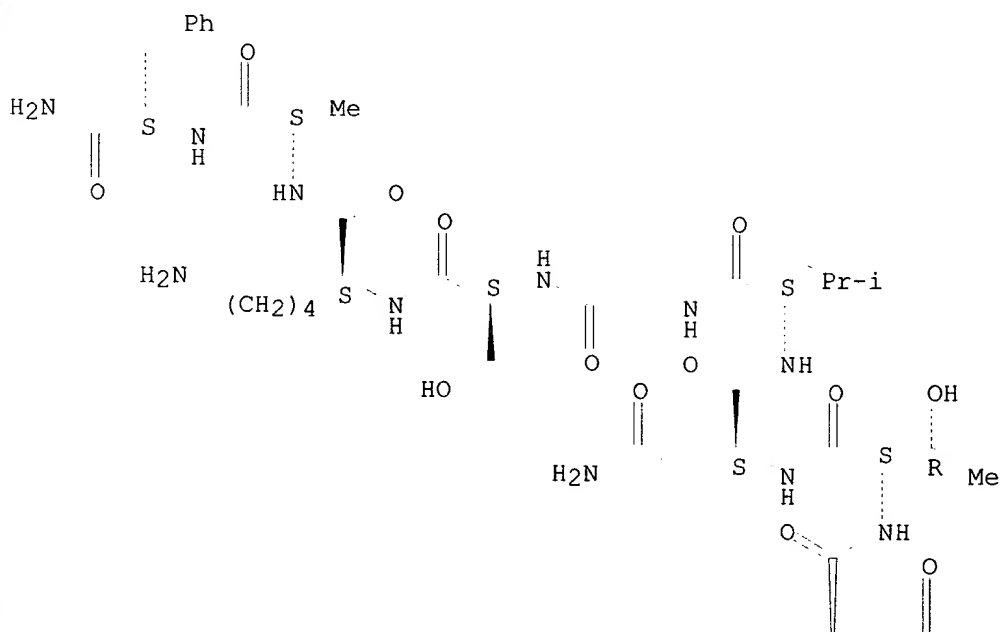


RN 226214-47-7 CAPLUS

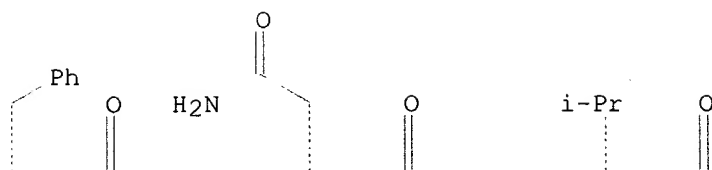
CN L-Phenylalaninamide, L-prolyl-L-threonyl-L-.alpha.-glutamyl-L-arginyl-L-leucyl-L-alanyl-L-.alpha.-glutamyl-L-leucyl-L-leucyl-L-seryl-L-arginyl-L-serylglycylglycyl-L-valyl-L-valyl-L-lysyl-L-asparaginyl-L-asparaginyl-L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-lysyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



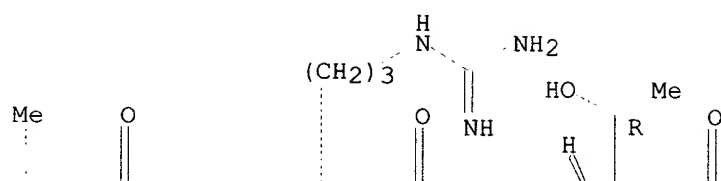
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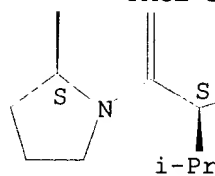
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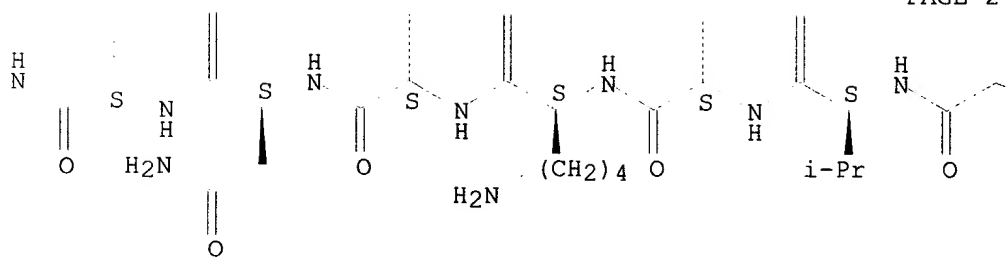
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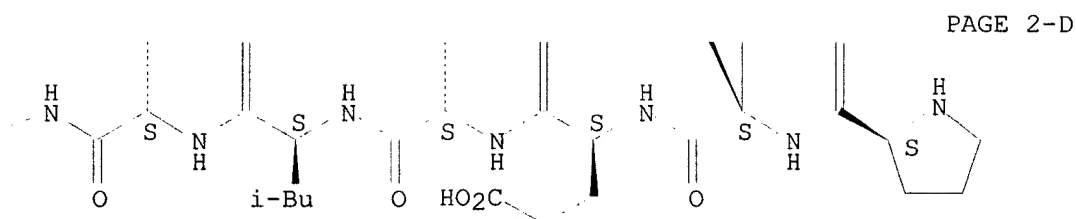
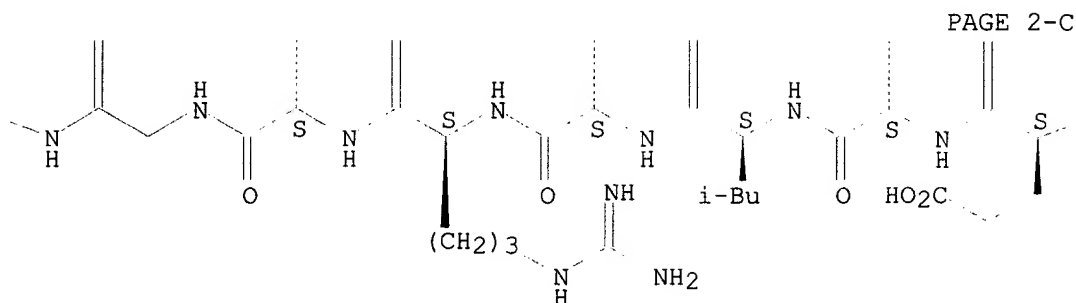


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PAGE 2-B





REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 13 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:135301 CAPLUS

DOCUMENT NUMBER: 132:289025

TITLE: The effects of a selective CGRP1 receptor antagonist, and a selective neuronal nitric oxide synthase inhibitor on neurogenic vasodilatation in the rat

AUTHOR(S): Towler, P. K.; Brain, S. D.

CORPORATE SOURCE: Pharmacology Group and Vascular Biology Research Centre, London, UK

SOURCE: Molecular Biology Intelligence Unit (2000), 10 (CGRP Family: Calcitonin Gene-Related Peptide (CGRP), Amylin, and Adrenomedullin), 217-218
CODEN: MBIUF8; ISSN: 1431-0414

PUBLISHER: R. G. Landes Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have studied the effects of CGRP8-37, and a selective neuronal nitric oxide (nNOS) inhibitor, 1-(2-trifluoromethylphenyl)imidazole (TRIM), on vasodilatation induced by stimulation of the rat saphenous nerve. TRIM significantly inhibits neurogenic vasodilatation induced by stimulation of the saphenous nerve. The authors suggest that this may be due to inhibition of the release of CGRP from nerve terminals, as NO is not thought to contribute to CGRP-induced vasodilatation.

IT 119911-68-1, 8-37-.alpha.-Calcitonin gene-related peptide (human)

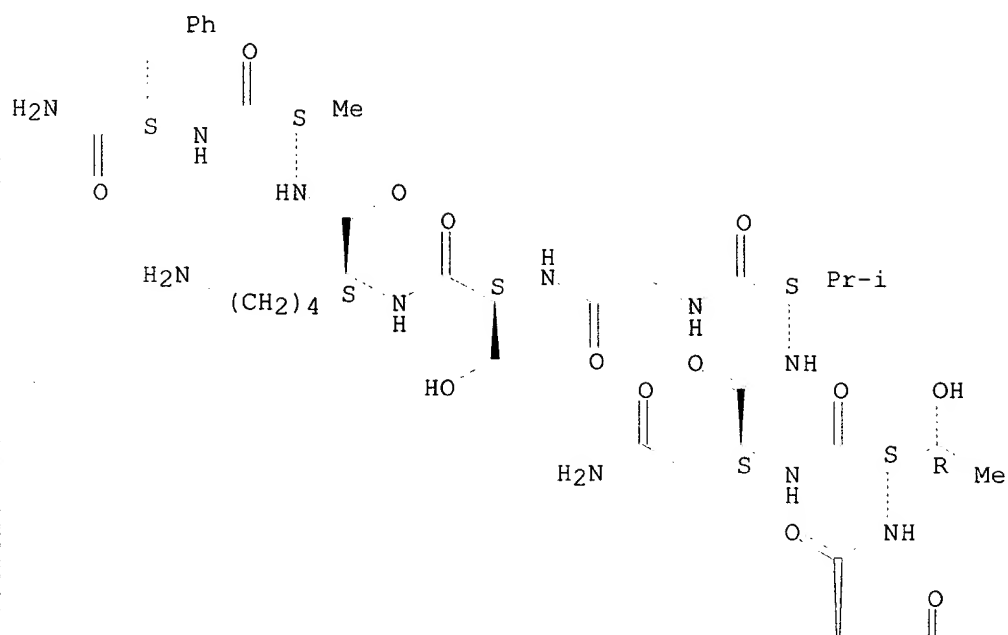
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(effects of selective CGRP1 receptor antagonist and selective neuronal nitric oxide synthase inhibitor on neurogenic vasodilatation in rat)

RN 119911-68-1 CAPLUS

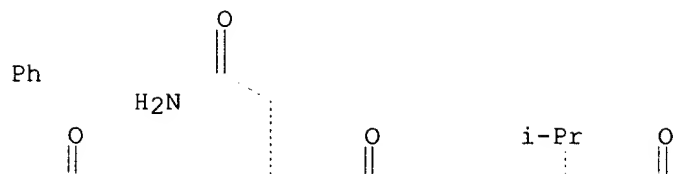
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



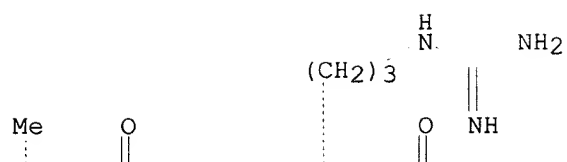
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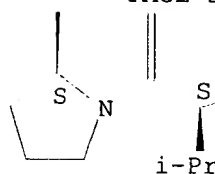
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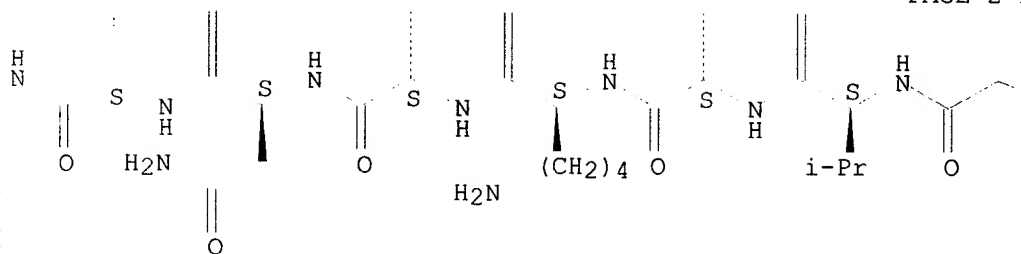
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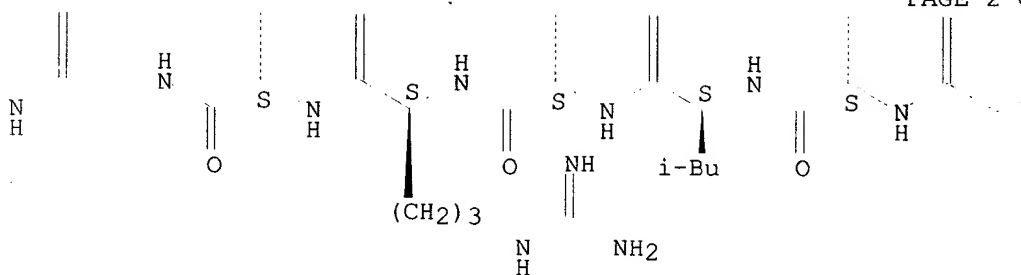
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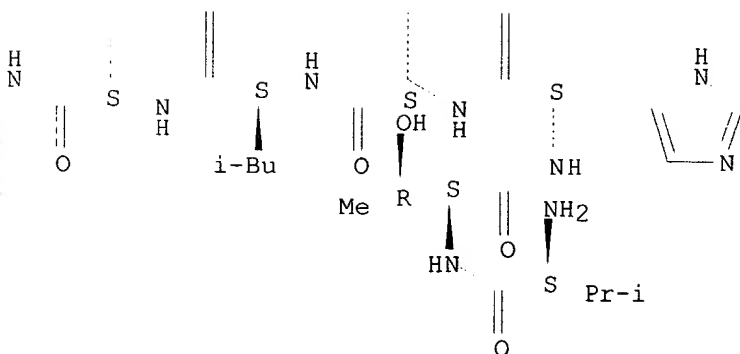
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REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 14 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:85895 CAPLUS

DOCUMENT NUMBER: 132:135966

Searched by Barb O'Bryen, STIC 308-4291

TITLE: Agonists of proteinase-activated receptor 2 induce inflammation by a neurogenic mechanism

AUTHOR(S): Steinhoff, M.; Vergnolle, N.; Young, S. H.; Tognetto, M.; Amadesi, S.; Ennes, H. S.; Trevisani, M.; Hollenberg, M. D.; Wallace, J. L.; Caughey, G. H.; Mitchell, S. E.; Williams, L. M.; Geppetti, P.; Mayer, E. A.; Bunnett, N. W.

CORPORATE SOURCE: Departments of Surgery and Physiology, University of California, San Francisco, CA, 94143, USA

SOURCE: Nature Medicine (New York) (2000), 6(2), 151-158
CODEN: NAMEFI; ISSN: 1078-8956

PUBLISHER: Nature America

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Trypsin and mast cell tryptase cleave proteinase-activated receptor 2 and, by unknown mechanisms, induce widespread inflammation. The authors found that a large proportion of primary spinal afferent neurons, which express proteinase-activated receptor 2, also contain the proinflammatory neuropeptides calcitonin gene-related peptide and substance P. Trypsin and tryptase directly signal to neurons to stimulate release of these neuropeptides, which mediate inflammatory edema induced by agonists of proteinase-activated receptor 2. This new mechanism of protease-induced neurogenic inflammation may contribute to the proinflammatory effects of mast cells in human disease. Thus, tryptase inhibitors and antagonists of proteinase-activated receptor 2 may be useful anti-inflammatory agents.

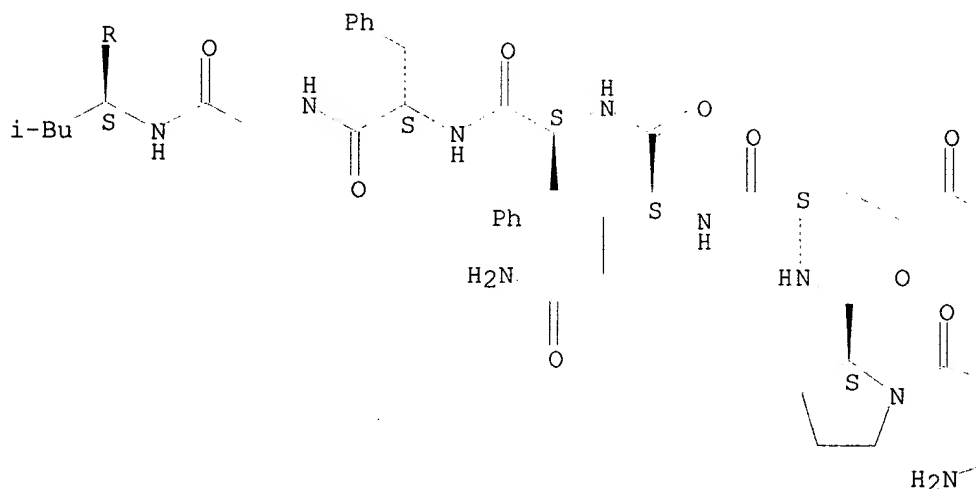
IT 33507-63-0, Substance P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(trypsin stimulated release of neuropeptides mediating inflammatory edema induced by PAR2)

RN 33507-63-0 CAPLUS

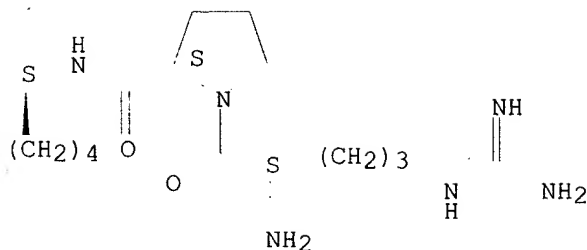
CN Substance P (9CI) (CA INDEX NAME)

Absolute stereochemistry.

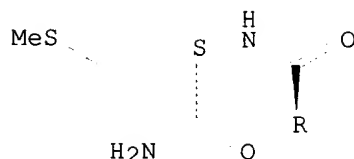
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NH₂

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REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 15 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:799643 CAPLUS

DOCUMENT NUMBER: 132:88528

TITLE: Adrenomedullin **receptor antagonism**

by **calcitonin gene-related**

peptide(8-37) inhibits carotid

artery neointimal hyperplasia after balloon injury

AUTHOR(S): Shimizu, Koichi; Tanaka, Hiroyuki; Sunamori, Makoto;

Marumo, Fumiaki; Shichiri, Masayoshi

CORPORATE SOURCE: Department of Cardiothoracic Surgery, Tokyo Medical

and Dental University, Tokyo, 113-8519, Japan

SOURCE: Circulation Research (1999), 85(12), 1199-1205

CODEN: CIRUAL; ISSN: 0009-7330

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Intimal injury by angioplasty results in a series of changes, including smooth muscle cell hyperplasia, that lead to vascular restenosis. Adrenomedullin, a potent vasodilator peptide, has natriuretic effects, and its plasma concn. is elevated in cardiovascular diseases. Adrenomedullin is secreted by endothelial and vascular smooth muscle cells, but its role in neointimal hyperplasia after balloon injury has not been previously described. The authors investigated the role of endogenous adrenomedullin in neointimal hyperplasia using an in vivo rat model of postinjury vascular restenosis. In the injured rats, bromodeoxyuridine-labeled

nuclei in the media of untreated common carotid arteries were increased 2 days after injury, which were suppressed by in vivo treatment with the adrenomedullin receptor antagonist calcitonin gene-related peptide (CGRP) (8-37). Inhibition of neointimal hyperplasia by CGRP(8-37) was distinct at 7 and 14 days, whereas CGRP(1-37) had no effect. The expression of adrenomedullin in the media of both untreated and treated common carotid arteries was elevated at 2 days and further enhanced in hyperplastic intima of untreated common carotid arteries at 7 days. The authors' findings suggest a novel role for endogenous adrenomedullin in balloon injury-induced restenosis and indicate that CGRP(8-37) may be useful for the prevention of vascular restenosis.

IT 119911-68-1, Human **calcitonin gene-related peptide 8-37**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

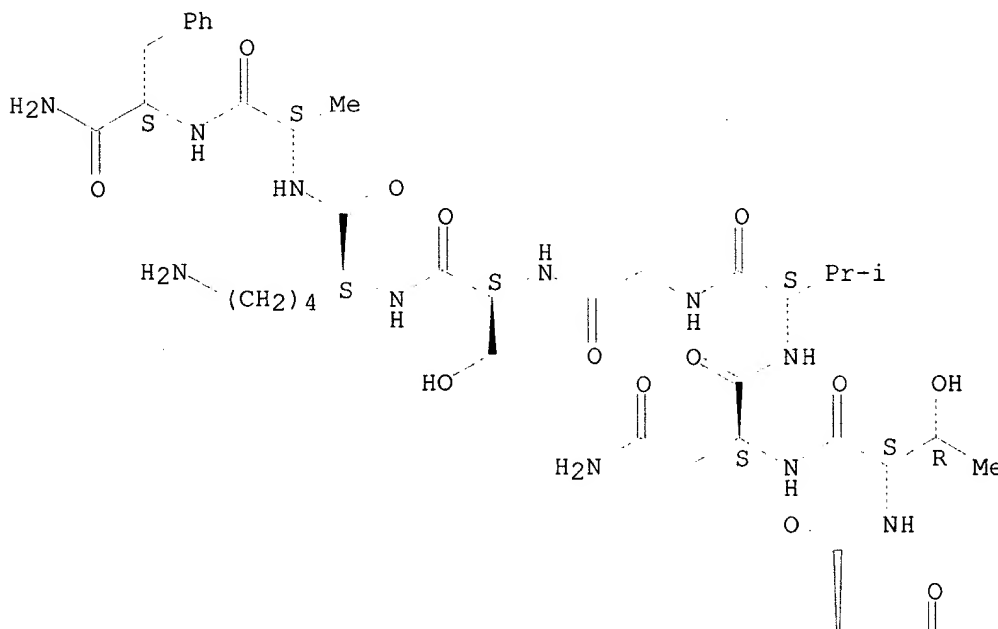
(adrenomedullin **receptor antagonism** by **calcitonin gene-related peptide (8-37) inhibits** carotid artery neointimal hyperplasia after balloon injury)

RN 119911-68-1 CAPLUS

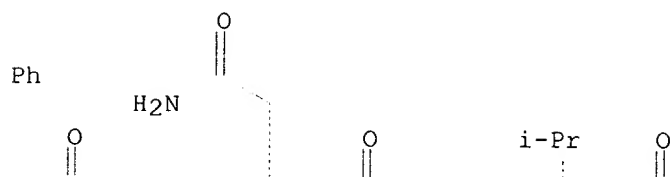
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



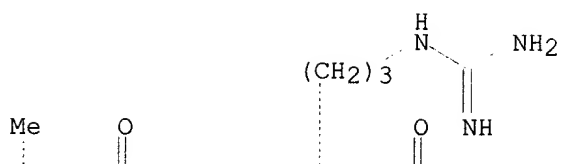
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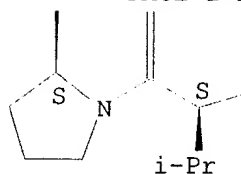
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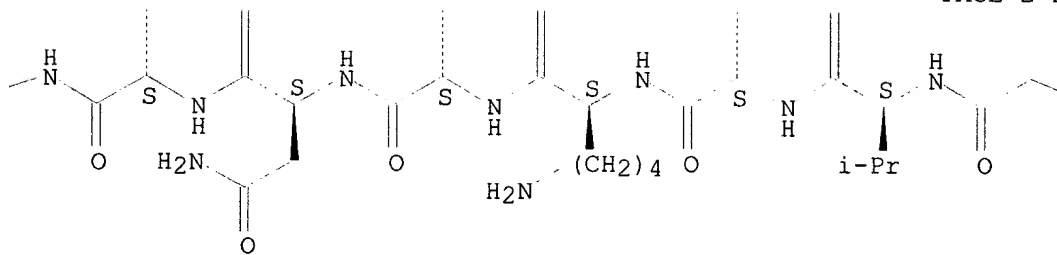
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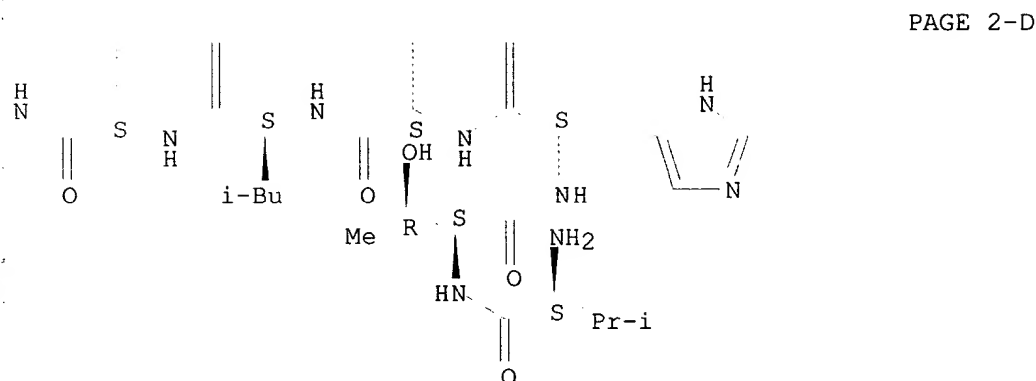
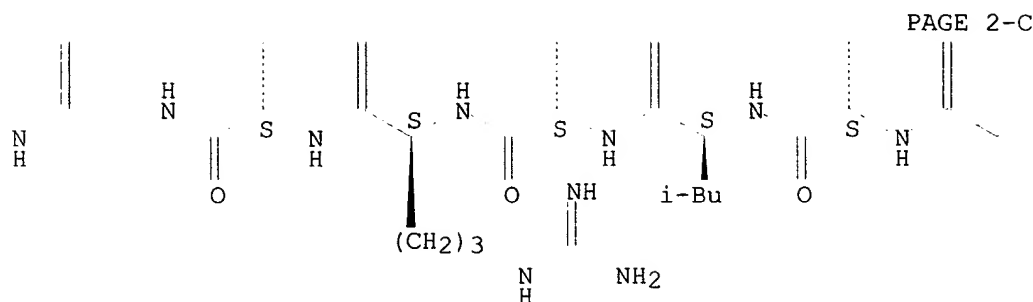


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REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 16 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:520198 CAPLUS

DOCUMENT NUMBER: 131:318097

TITLE: **Calcitonin gene-related**

peptide 8-37 inhibits the evoked discharge frequency of wide dynamic range neurons in dorsal horn of the spinal cord in rats

AUTHOR(S): Yu, L.-C.; Zheng, E.-M.; Lundberg, T.

CORPORATE SOURCE: College of Life Science, Department of Physiology, Peking University, Beijing, Peop. Rep. China

SOURCE: Regulatory Peptides (1999), 83(1), 21-24

CODEN: REPPDY; ISSN: 0167-0115

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The present study was performed to explore the effect of calcitonin gene-related peptide 8-37 (CGRP8-37) on the elec. stimulation-evoked discharge frequency of wide dynamic range (WDR) neurons in the dorsal horn of the spinal cord in rats. The discharge frequencies of WDR neurons were evoked by transdermic elec. stimulation applied on the ipsilateral hindpaw. CGRP8-37 was applied directly on the dorsal surface of the L3 to L5 spinal cord. After the administration of 3 nmol of CGRP8-37, the evoked discharge frequency of WDR neurons decreased significantly, an effect lasting more than 30 min. The results indicate that CGRP receptors play an important role in the transmission of presumed nociceptive information in the dorsal horn of the spinal cord.

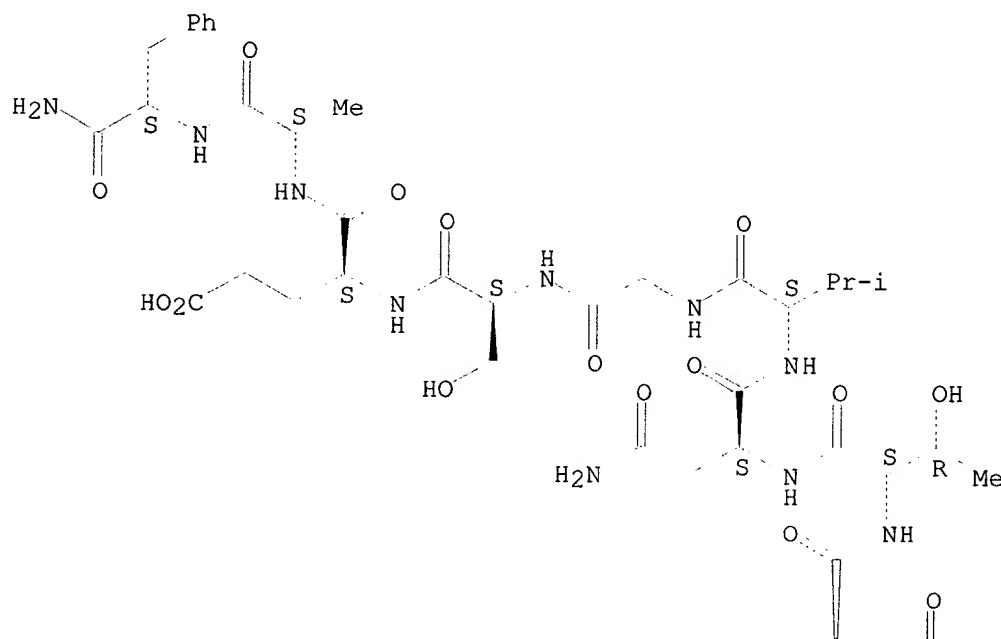
IT 129121-73-9, Rat **Calcitonin gene-related peptide 8-37**

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); BIOL (Biological study)
(**calcitonin gene-related peptide**
8-37 **inhibits** evoked discharge frequency of wide dynamic
range neurons in dorsal horn of spinal cord in rat)

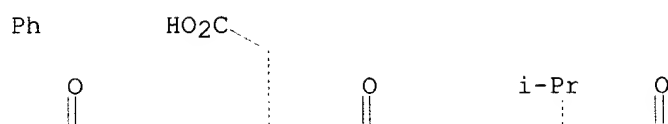
RN 129121-73-9 CAPLUS
CN 8-37-.alpha.-Calcitonin gene-related peptide (rat reduced) (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



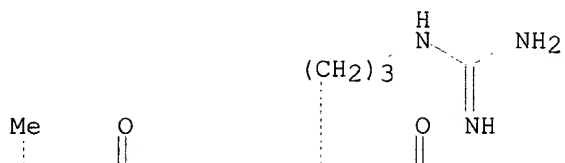
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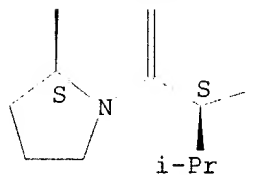
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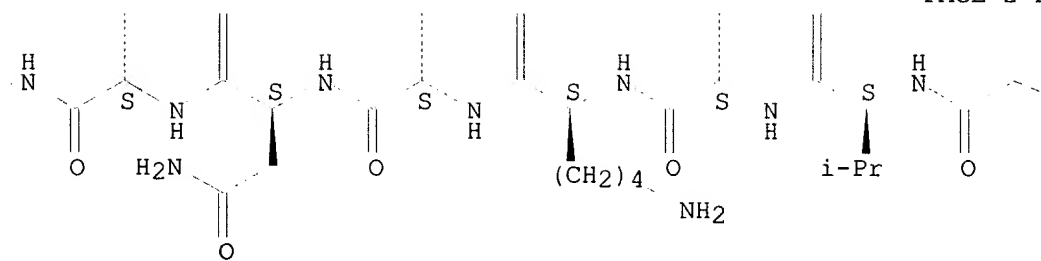
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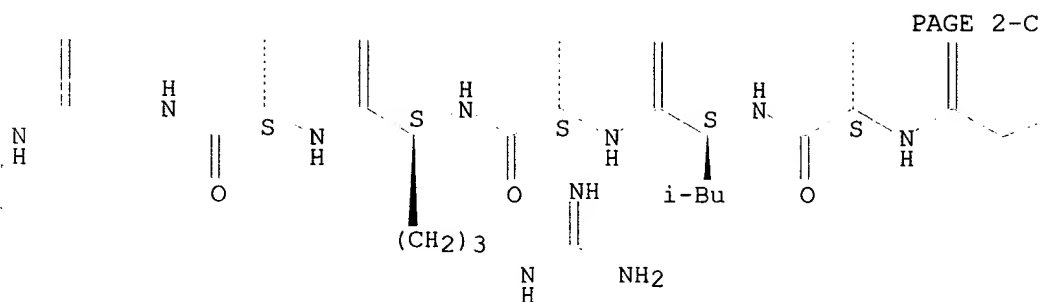


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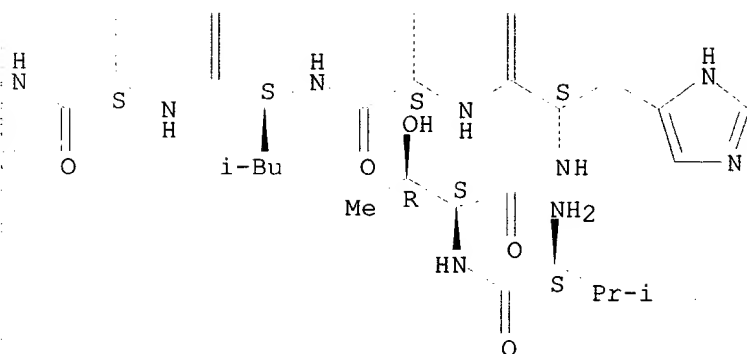


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REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 17 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:396668 CAPLUS

DOCUMENT NUMBER: 131:209289

TITLE: [D-Pen_{2,7}]-human-.alpha.-calcitonin

gene-related peptide: a

novel CGRP antagonist

AUTHOR(S): Smith, D. David; Saha, Shankar; Waugh, David J. J.; Abel, Peter W.

CORPORATE SOURCE: Department of Biomedical Sciences, Creighton University, Omaha, NE, 68178, USA

SOURCE: Peptides: Frontiers of Peptide Science, Proceedings of the American Peptide Symposium, 15th, Nashville, June 14-19, 1997 (1999), Meeting Date 1997, 597-598.

Editor(s): Tam, James P.; Kaumaya, Pravin T. P.

Kluwer: Dordrecht, Neth.

CODEN: 67UCAR

DOCUMENT TYPE: Conference

LANGUAGE: English

AB To examine the effect of conformationally constraining the disulfide bridge the authors report the synthesis, binding and functional properties of CGRP analogs contg. L/D-Pen residues in positions 2 and/or 7. The binding affinity of each analog was detd. as its ability to inhibit ¹²⁵I-h-.alpha.-CGRP binding to membranes prepd. from pig coronary arteries and functional expts. detd. each analog's ability to relax pig coronary arteries. h-.alpha.-CGRP caused relaxation of coronary arteries and bound to G-protein coupled and uncoupled states of the receptor. [Pen₂]h-.alpha.-CGRP was an equipotent full agonist with the same affinity as h-.alpha.-CGRP for the CGRP receptor. Changing the configuration of

Pen only caused minor redns. in potency and affinity. However, a Pen residue in position 7 resulted in significant redns. in potency and binding affinity. Furthermore, [D-Pen7]h-.alpha.-CGRP, rather than showing any agonist effects, was a weak antagonist. All [D-Pen7]-contg. analogs were antagonists of which [D-Pen2,7]h-.alpha.-CGRP had the highest affinity. Binding and functional properties of the disubstituted Pen analogs were consistent with those of the monosubstituted Pen analogs. Substitution of Cys for D-Pen abolishes agonist effects of h-.alpha.-CGRP and produces an antagonist. The most potent antagonist, [D-Pen2'7]h-.alpha.-CGRP, has an affinity for CGRP receptors similar to that of h-.alpha.-CGRP (8-37).

IT 119911-68-1, 8-37-.alpha.-Calcitonin gene-related peptide (human)

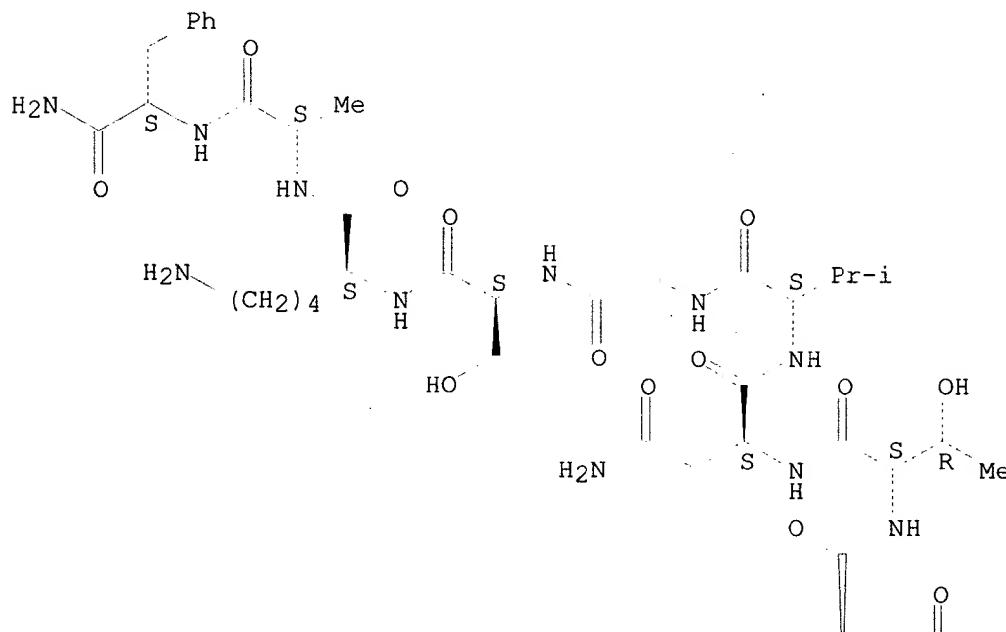
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(CGRP analog agonist and antagonist activity in relation to structure)

RN 119911-68-1 CAPLUS

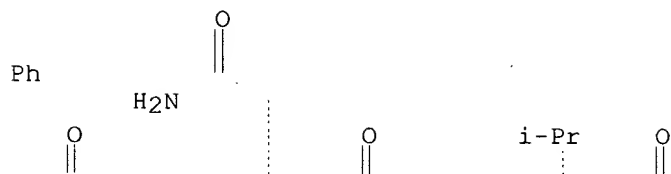
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



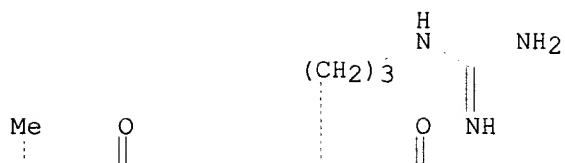
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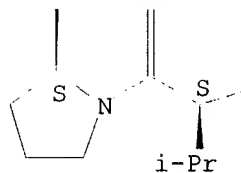
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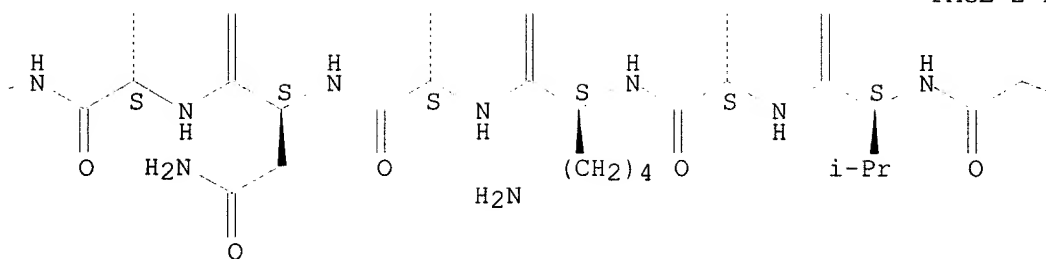
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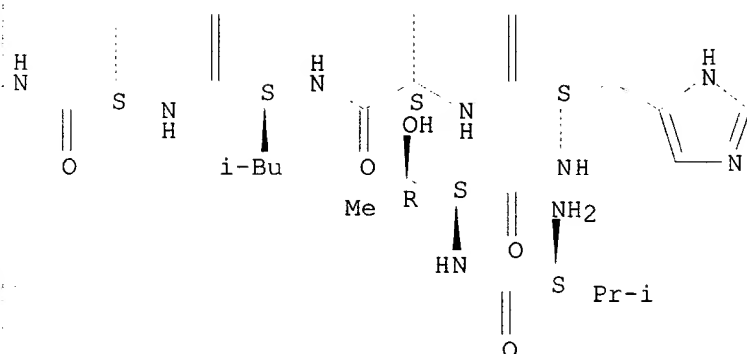
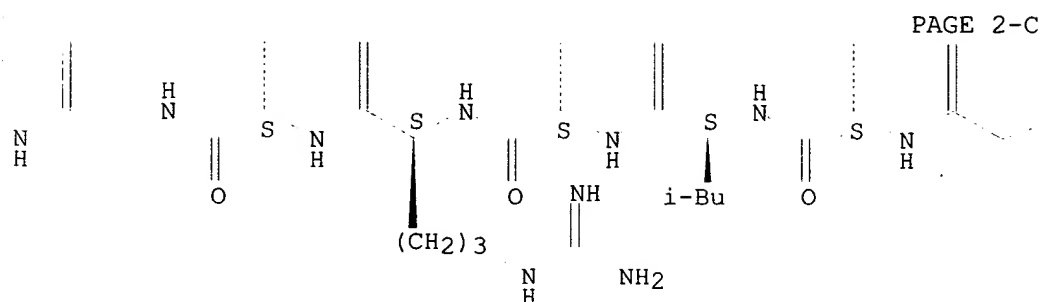


PAGE 2-A



PAGE 2-B





REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 18 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:113128 CAPLUS

DOCUMENT NUMBER: 130:347514

TITLE: CGRP 27-37 analogs with high affinity to the CGRP1 receptor show antagonistic properties in a rat blood flow assay

AUTHOR(S): Rist, Beate; Lacroix, J. Silvain; Entzeroth, Michael; Doods, Henry N.; Beck-Sickinger, Annette G.

CORPORATE SOURCE: ETH Zurich, Department of Pharmacy, Winterthurer Str. 190, Zurich, CH 8057, Switz.

SOURCE: Regulatory Peptides (1999), 79(2,3), 153-158
CODEN: REPPDY; ISSN: 0167-0115

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB CGRP Y0-28-37 is known as a selective CGRP1 receptor antagonist. We succeeded in optimizing the CGRP1 receptor affinity of this fragment by multiple amino acid replacement. The analogs [P34, F35]CGRP 27-37 and [D31, P34, F35]CGRP 27-37 exhibit a 100-fold increased affinity compared to the unmodified segment. Receptor binding studies were performed with human neuroblastoma cells SK-N-MC, which selectively express the hCGRP1 receptor. Blood flow, which is increased by exogenous CGRP, was measured in the right femoral artery. Preincubation of the rats with [P34, F35]CGRP 27-37 and [D31, P34, F35]CGRP 27-37 led to a significant decrease in CGRP induced increase in vascular conductance indicating the antagonistic properties of these compds. Interestingly, an exchange of the amino acid Asn31 to Asp31 in [P34, F35]CGRP 27-37 shortened the period of the antagonistic effect significantly, suggestive of a different rate

of metab. for the two ligands. Secondary structure investigations obtained by CD measurements revealed that an increase in ordered structure correlates with high binding affinity.

IT 224639-29-6 224639-36-5 224639-42-3
224639-47-8 224639-53-6 224639-58-1

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

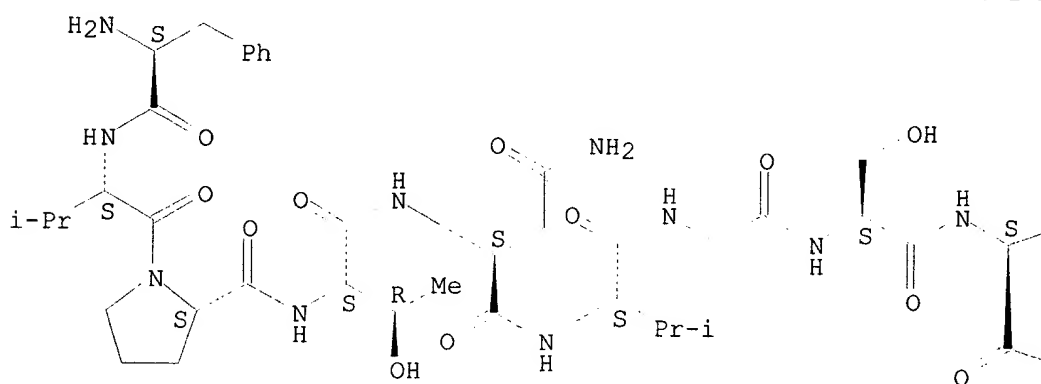
(CGRP 27-37 analogs with high affinity to CGRP1 receptor show antagonistic properties in a rat blood flow assay)

RN 224639-29-6 CAPLUS

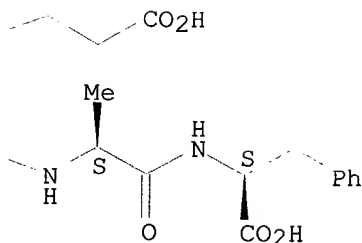
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-.alpha.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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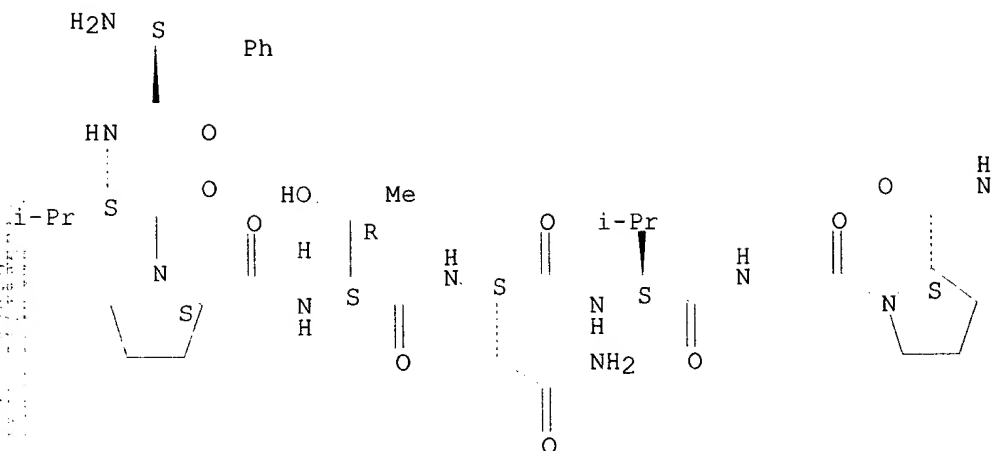


RN 224639-36-5 CAPLUS

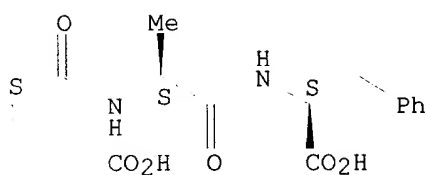
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-prolyl-L-.alpha.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



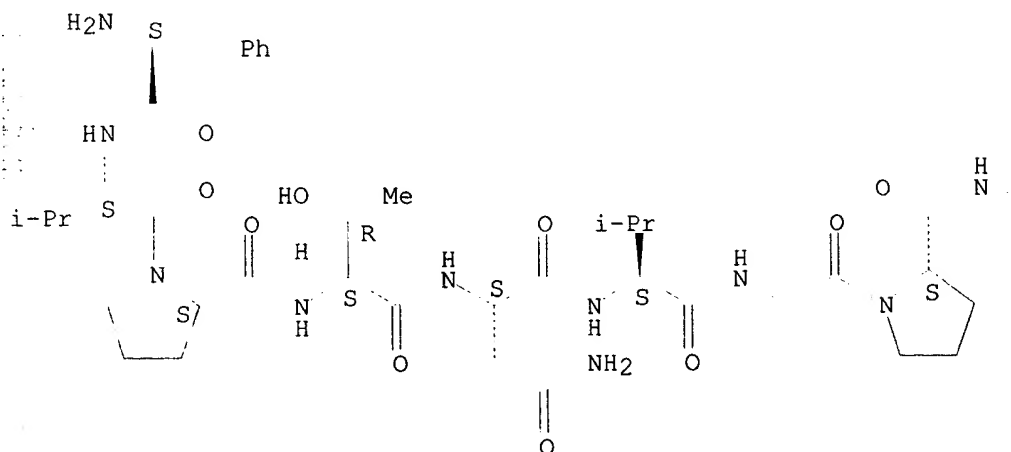
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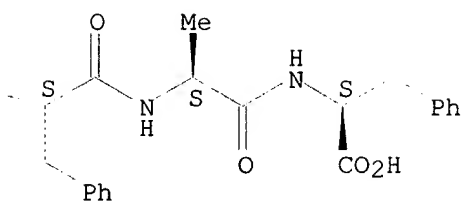
224639-42-3 CAPLUS
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L-valylglycyl-L-prolyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

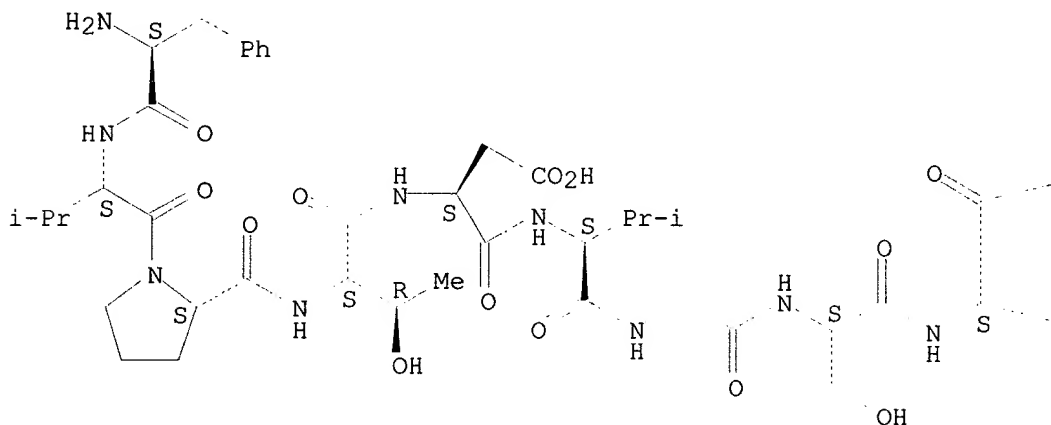


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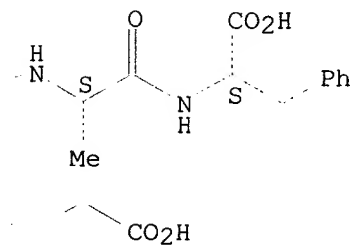
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
aspartyl-L-valylglycyl-L-seryl-L-.alpha.-glutamyl-L-alanyl- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

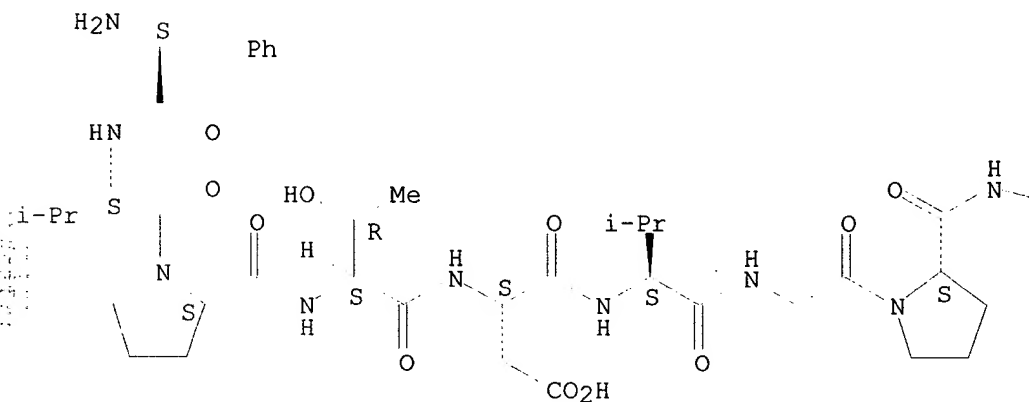


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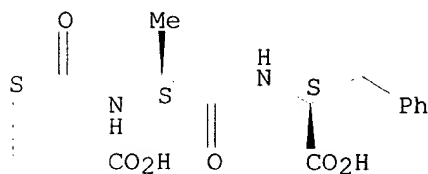
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
aspartyl-L-valylglycyl-L-prolyl-L-.alpha.-glutamyl-L-alanyl- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



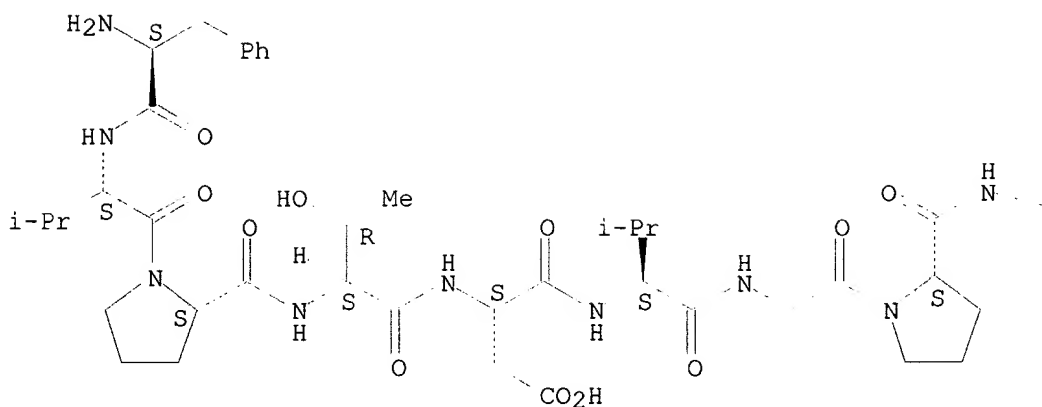
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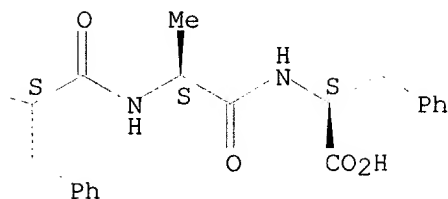
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NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 19 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:96518 CAPLUS

DOCUMENT NUMBER: 130:153978

TITLE: Solid-phase synthesis of peptide **CGRP-antagonists** for use as medicaments

INVENTOR(S): Beck-Sickinger, Annette; Rist, Beate; Entzeroth, Michael

PATENT ASSIGNEE(S): Dr. Karl Thomae G.m.b.H., Germany

SOURCE: Ger. Offen., 20 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19732944	A1	19990204	DE 1997-19732944	19970731

OTHER SOURCE(S): MARPAT 130:153978

AB Variations on the r-CGRP-alpha-27-37 partial sequence H-F27-V28-P29-T30-N31-V32-G33-S34-E35-A36-F37-NH2 (see text for specifications) were prepd. using solid-phase peptide synthesis techniques, for use in acute and prophylactic treatment of headache, non-insulin-dependent diabetes mellitus, cardiovascular disease, skin disease, inflammatory disease,

allergic rhinitis, asthma, clotting disorders, and morphine tolerance (no data).

IT

80705-22-2P 115833-79-9P 129693-73-8P

201612-69-3P 201612-78-4P 201612-79-5P

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RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL

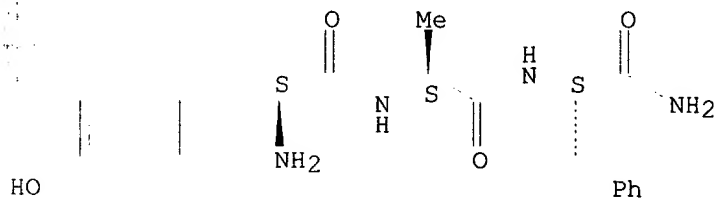
(Biological study); PREP (Preparation); USES (Uses)

(prepn. of via solid-phase synthesis as CGRP-
antagonists for use as medicaments)

RN 80705-22-2 CAPLUS

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Absolute stereochemistry.

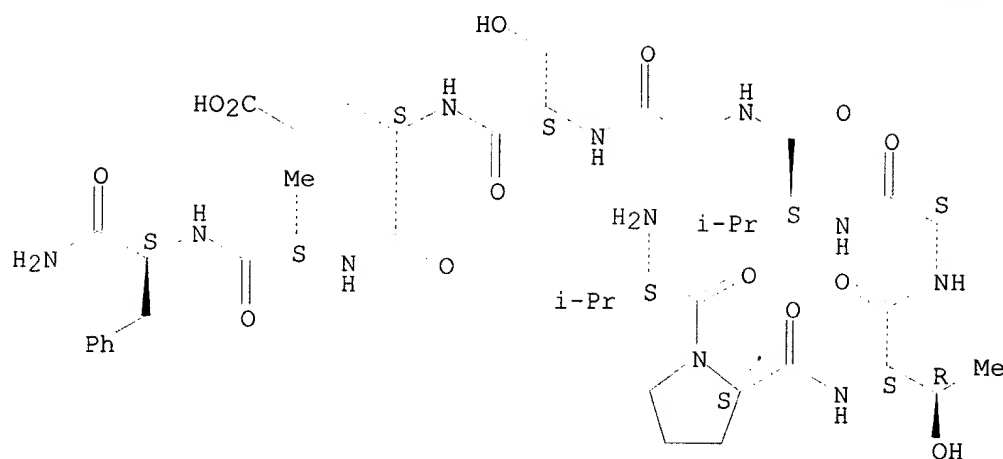


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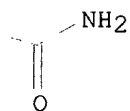
CN L-Phenylalaninamide, L-valyl-L-prolyl-L-threonyl-L-asparaginyll-L-valylglycyl-L-seryl-L-.alpha.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

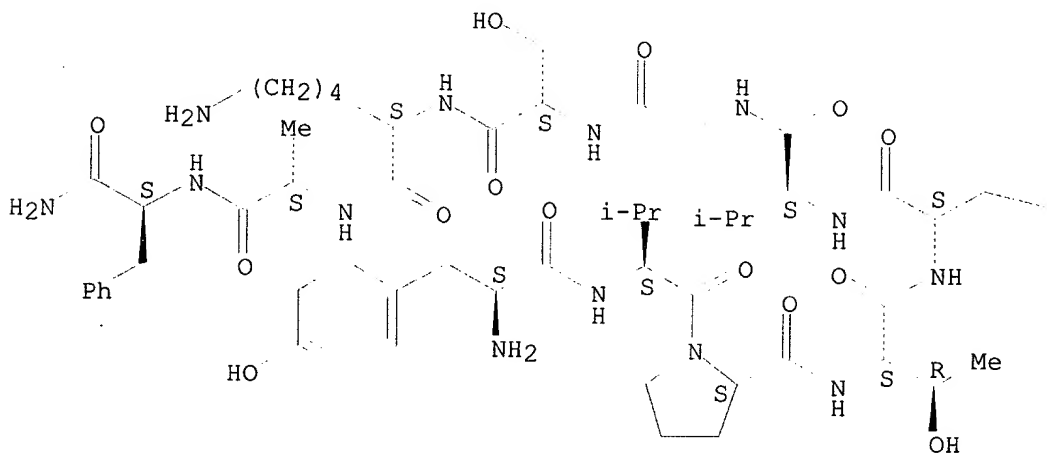


RN 129693-73-8 CAPLUS

CN L-Phenylalaninamide, L-tyrosyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyll-L-valylglycyl-L-seryl-L-lysyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

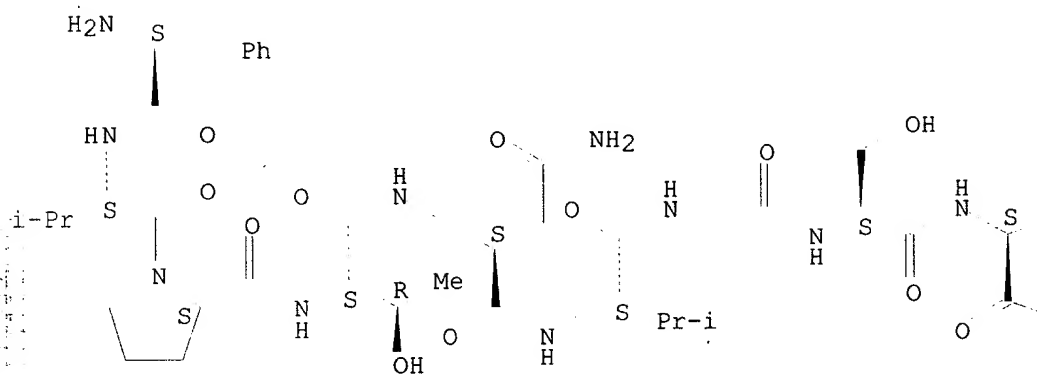
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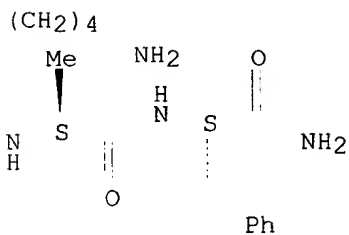
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Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

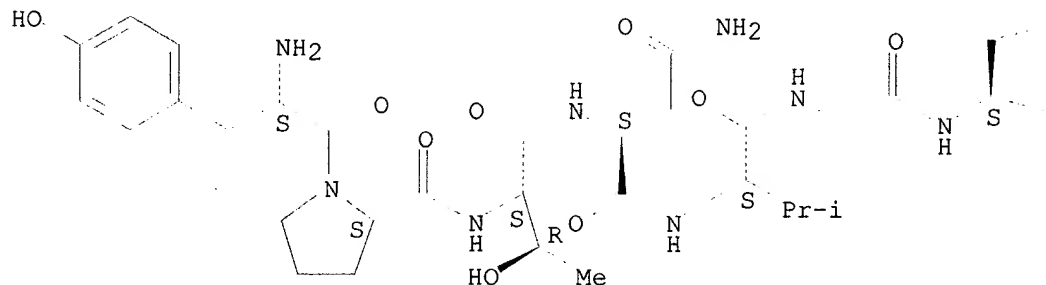


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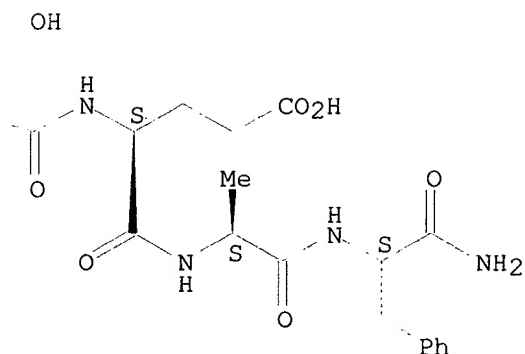
CN L-Phenylalaninamide, L-tyrosyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-.alpha.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

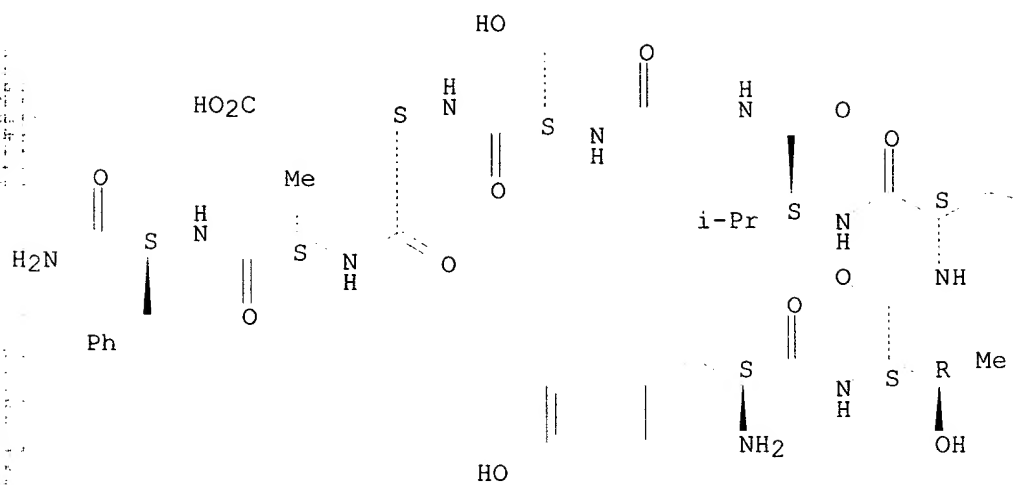


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Absolute stereochemistry.

PAGE 1-A

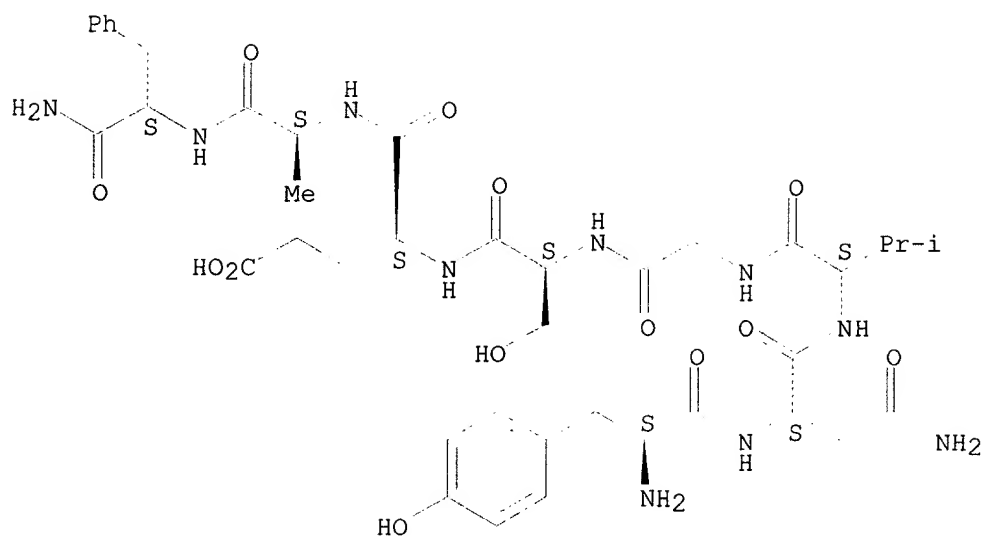


PAGE 1-B

NH₂

RN 201612-80-8 CAPLUS
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 .alpha.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

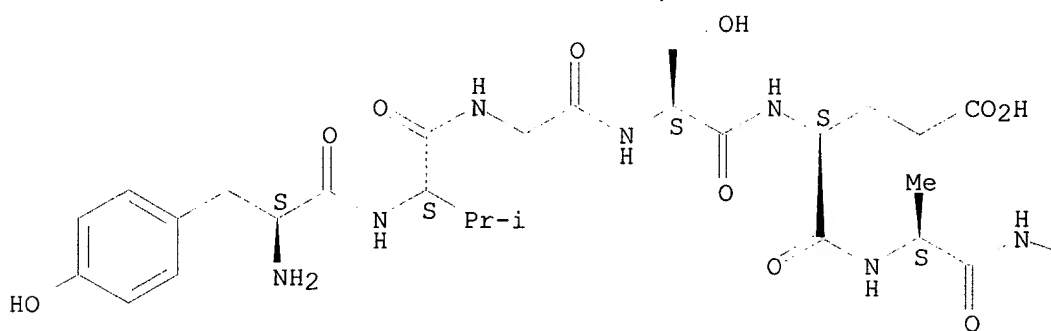


RN 201612-81-9 CAPLUS

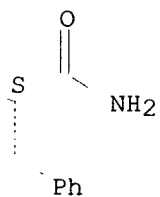
CN L-Phenylalanyl-L-tyrosyl-L-valylglycyl-L-seryl-L- α -glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



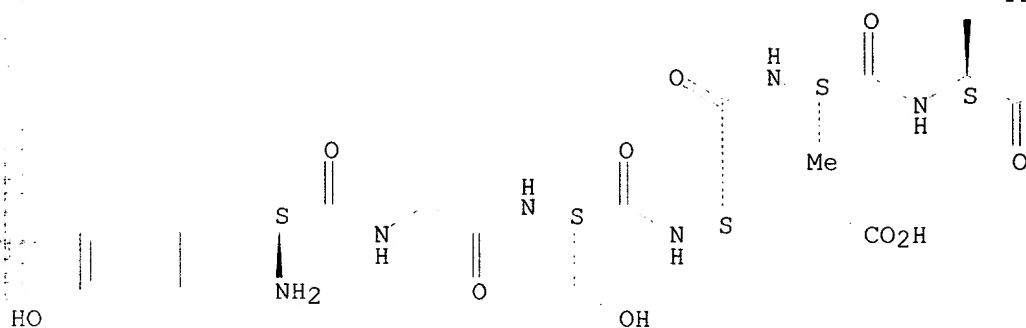
RN 201612-82-0 CAPLUS

CN L-Phenylalaninamide, L-tyrosylglycyl-L-seryl-L-.alpha.-glutamyl-L-alanyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

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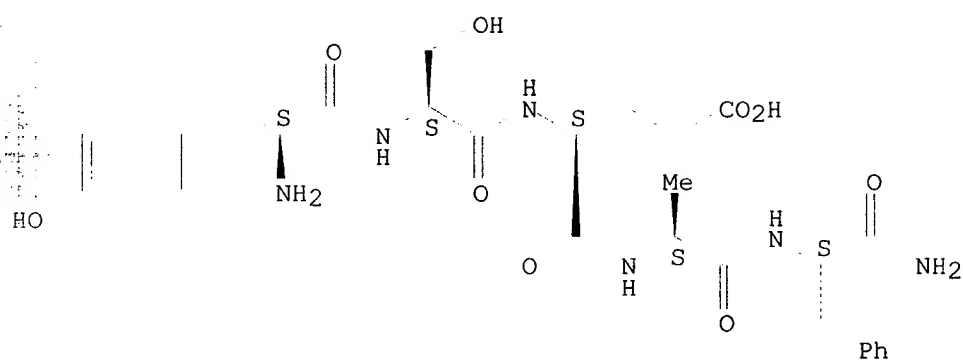


PAGE 1-B

NH₂

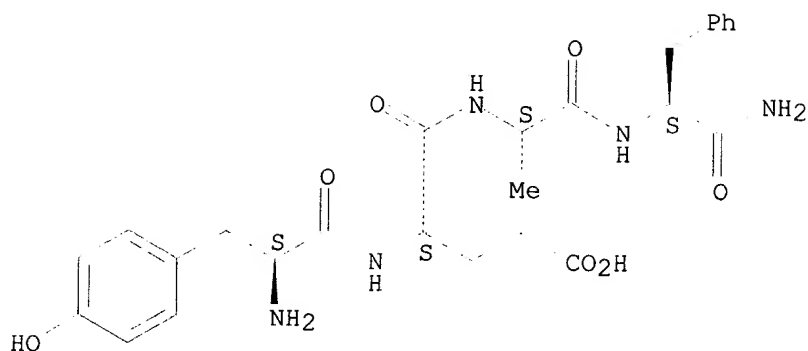
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CN L-Phenylalaninamide, L-tyrosyl-L-seryl-L-.alpha.-glutamyl-L-alanyl- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



RN 201612-84-2 CAPLUS
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INDEX NAME)

Absolute stereochemistry.

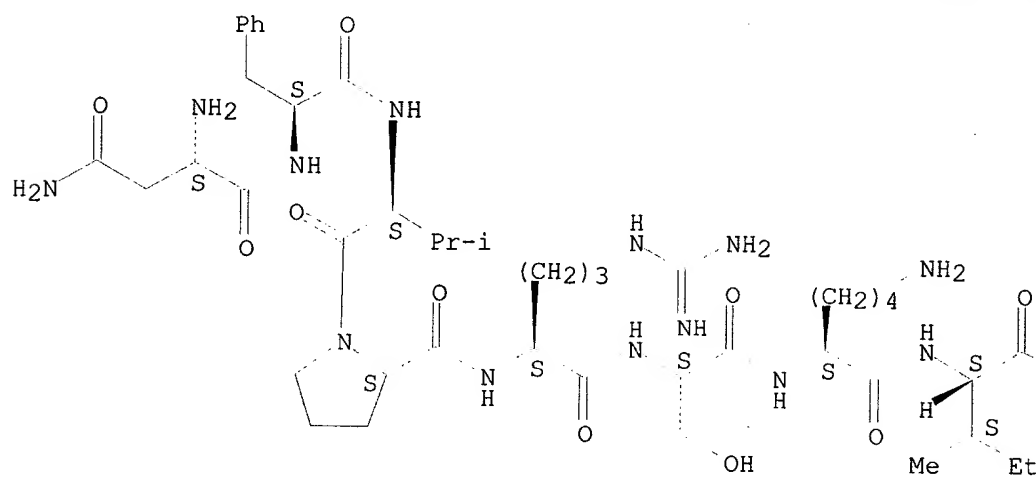


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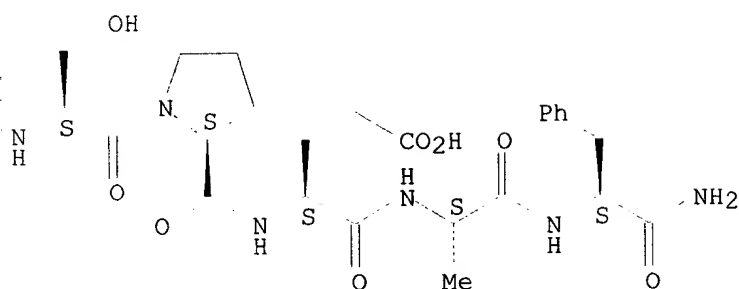
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Absolute stereochemistry.

PAGE 1-A



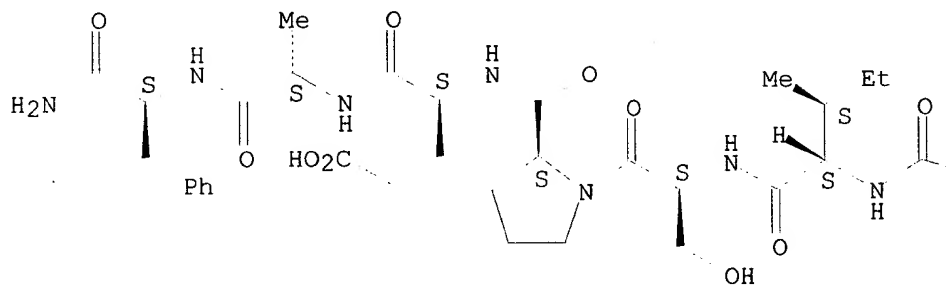
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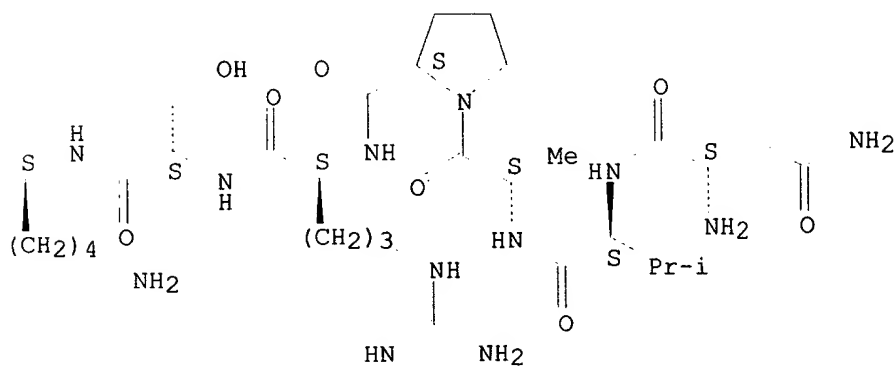
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Absolute stereochemistry.

PAGE 1-A



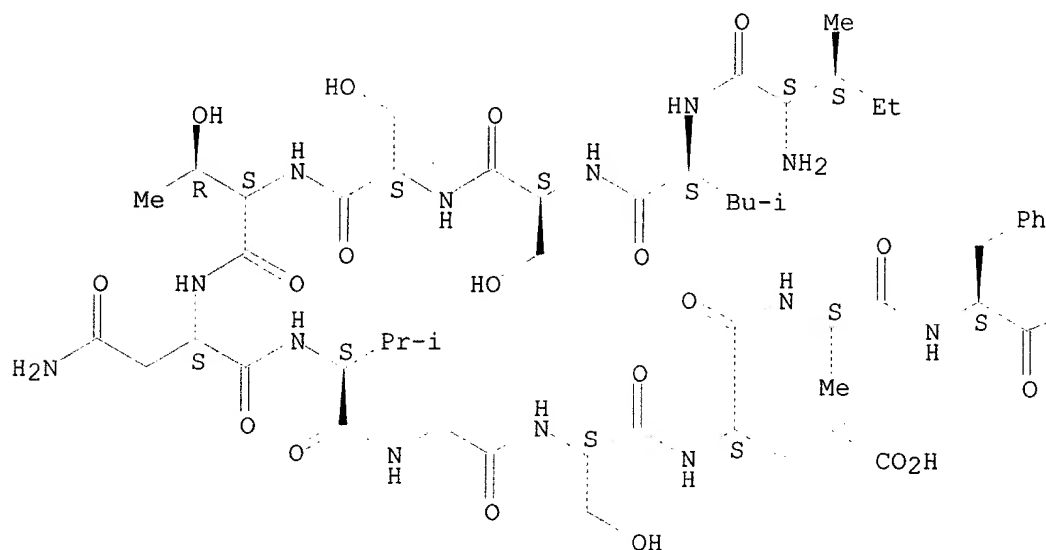
PAGE 1-B



RN 201612-92-2 CAPLUS
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Absolute stereochemistry.

PAGE 1-A



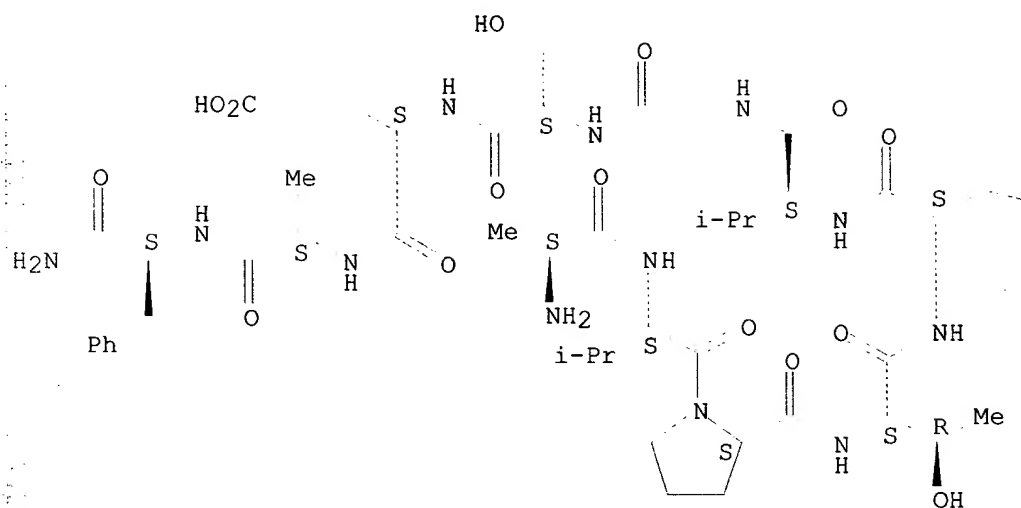
PAGE 1-B

NH2

RN 201612-93-3 CAPLUS
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Absolute stereochemistry.

PAGE 1-A



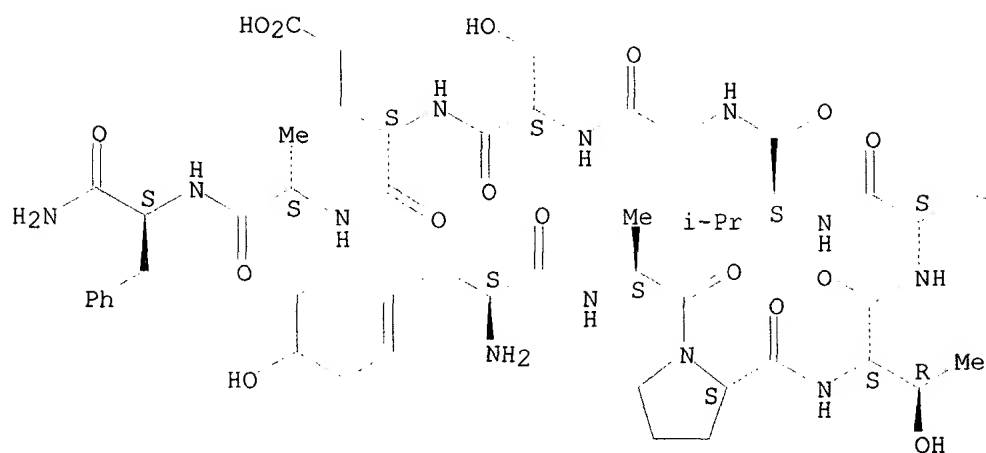
PAGE 1-B

NH₂

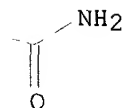
RN 201612-94-4 CAPLUS
 CN L-Phenylalaninamide, L-tyrosyl-L-alanyl-L-prolyl-L-threonyl-L-asparaginyll-
 L-valylglycyl-L-seryl-L-.alpha.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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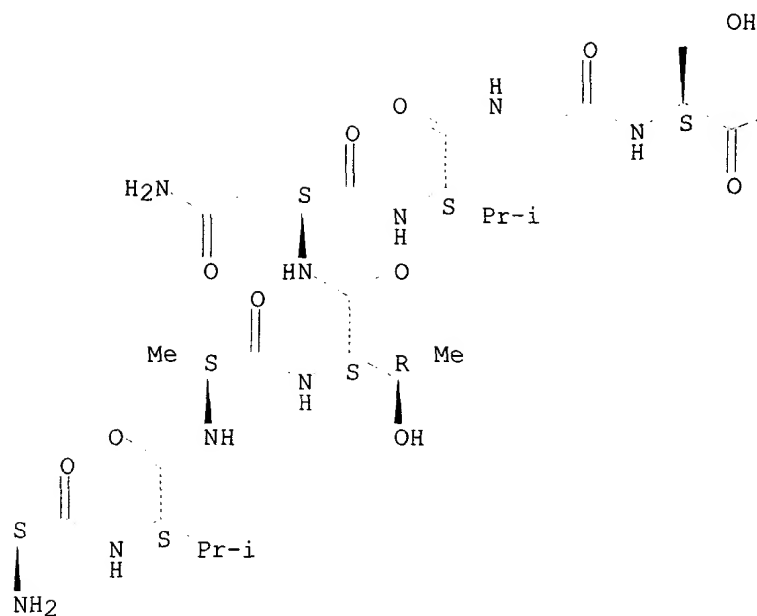
PAGE 1-B



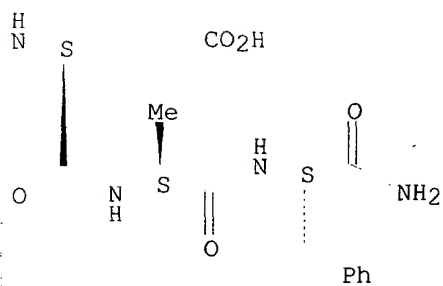
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Absolute stereochemistry.

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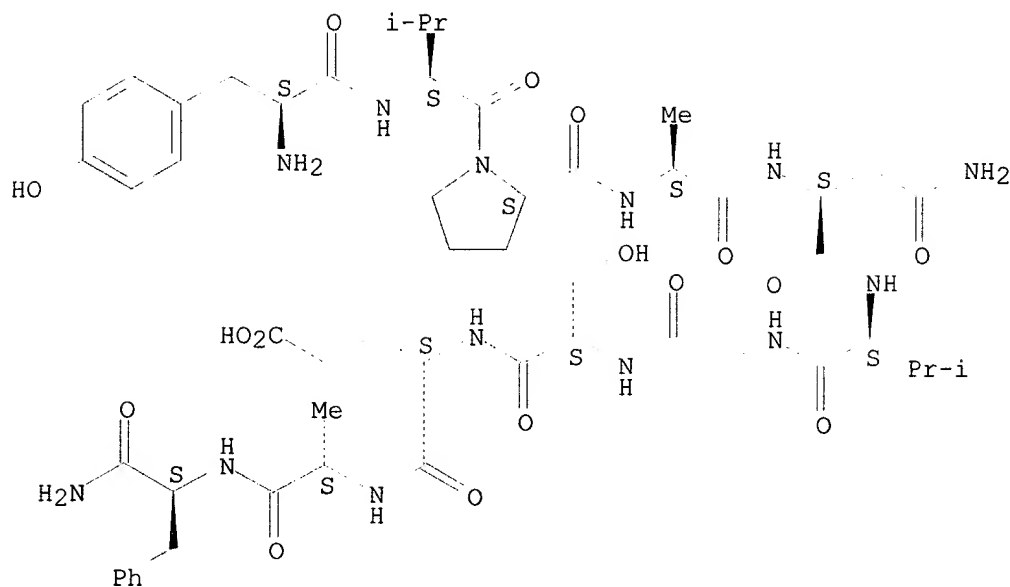
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HO

RN 201612-96-6 CAPLUS

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Absolute stereochemistry.

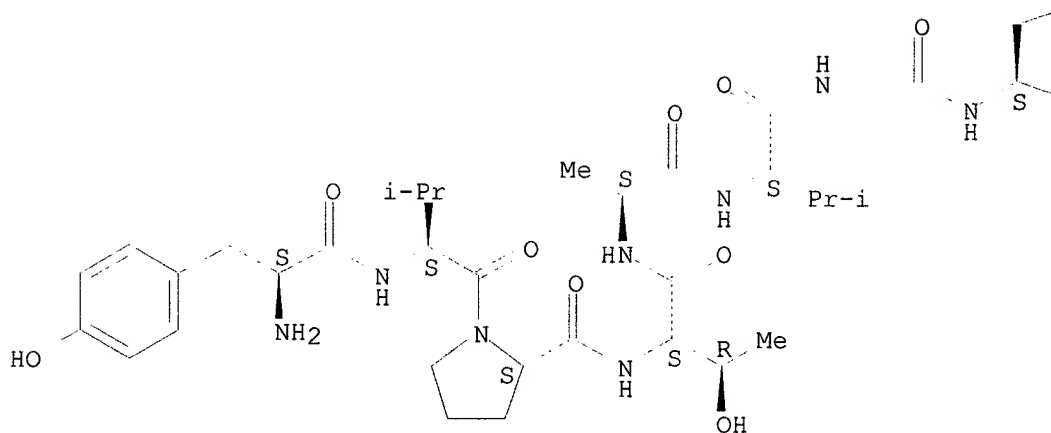


RN 201612-97-7 CAPLUS

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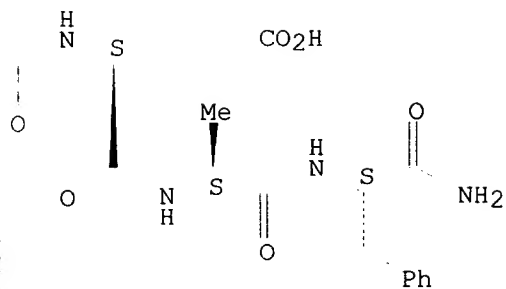
Absolute stereochemistry.

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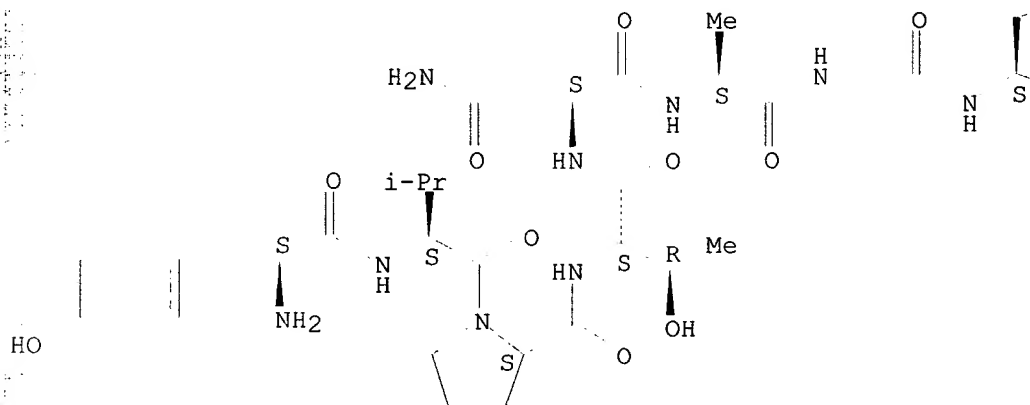
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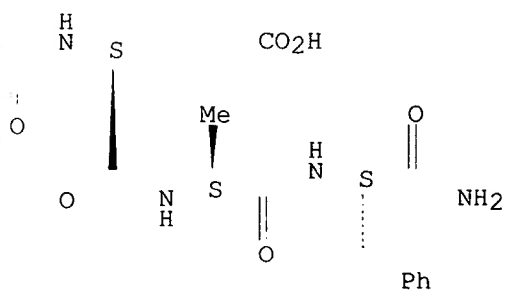
Absolute stereochemistry.

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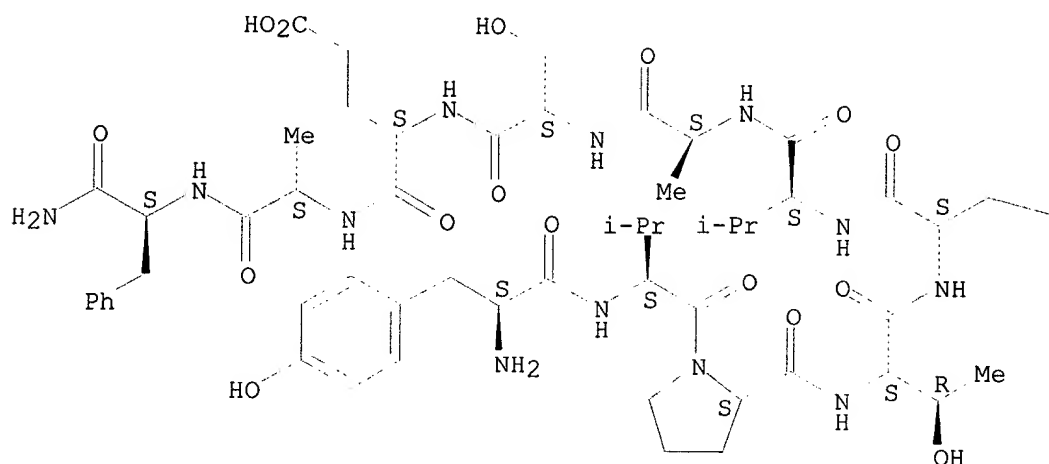


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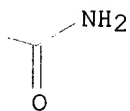
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Absolute stereochemistry.

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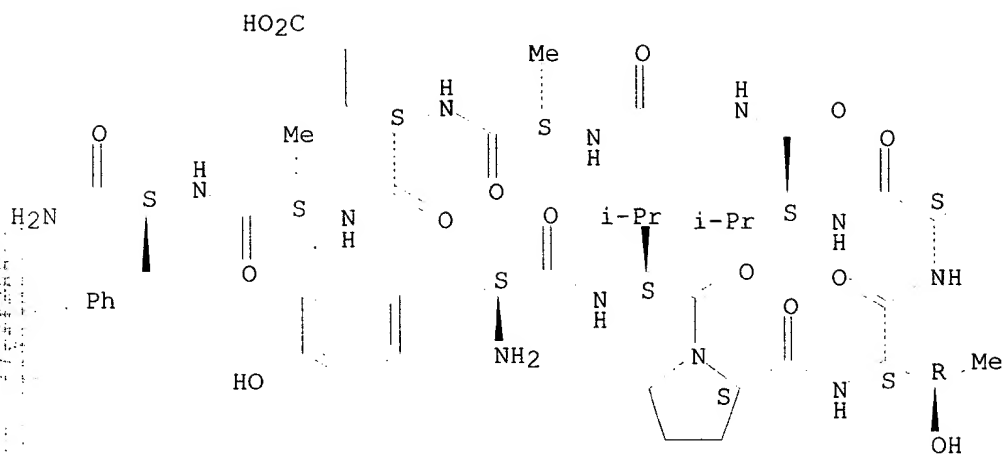


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Absolute stereochemistry.

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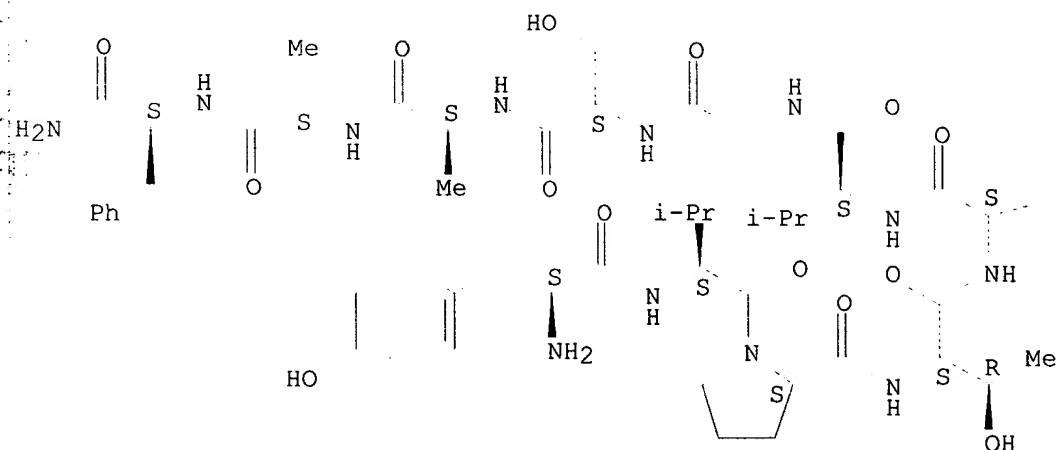
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NH₂

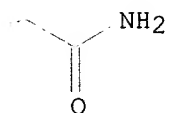
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Absolute stereochemistry.

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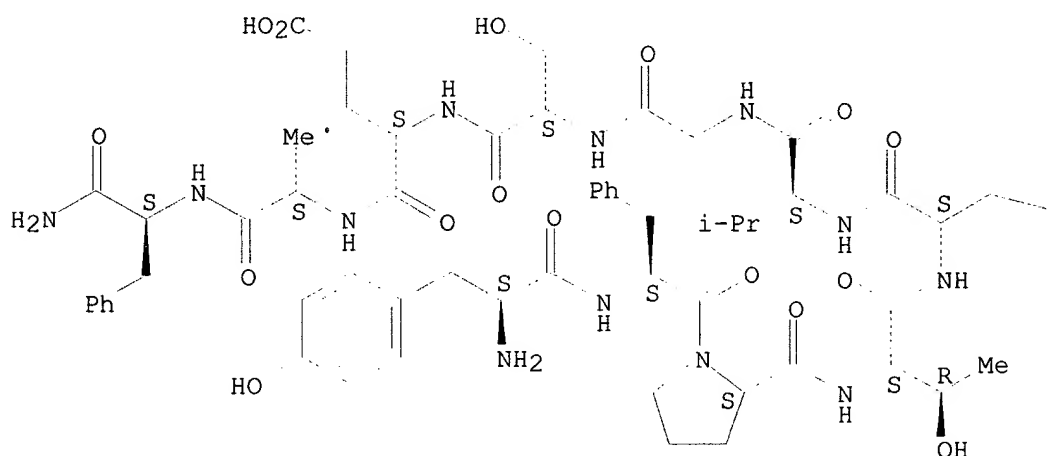
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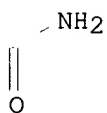
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Absolute stereochemistry.

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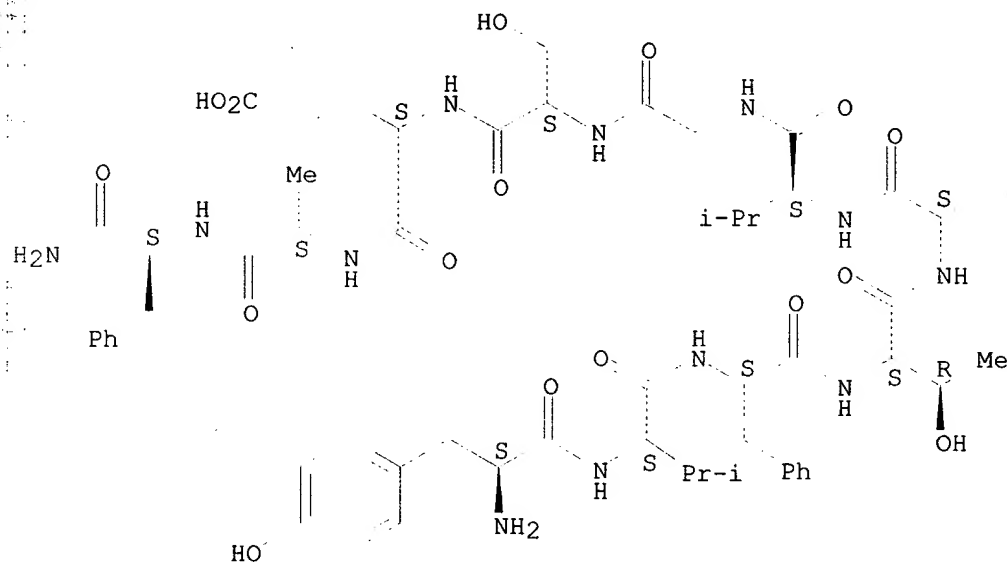


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Absolute stereochemistry.

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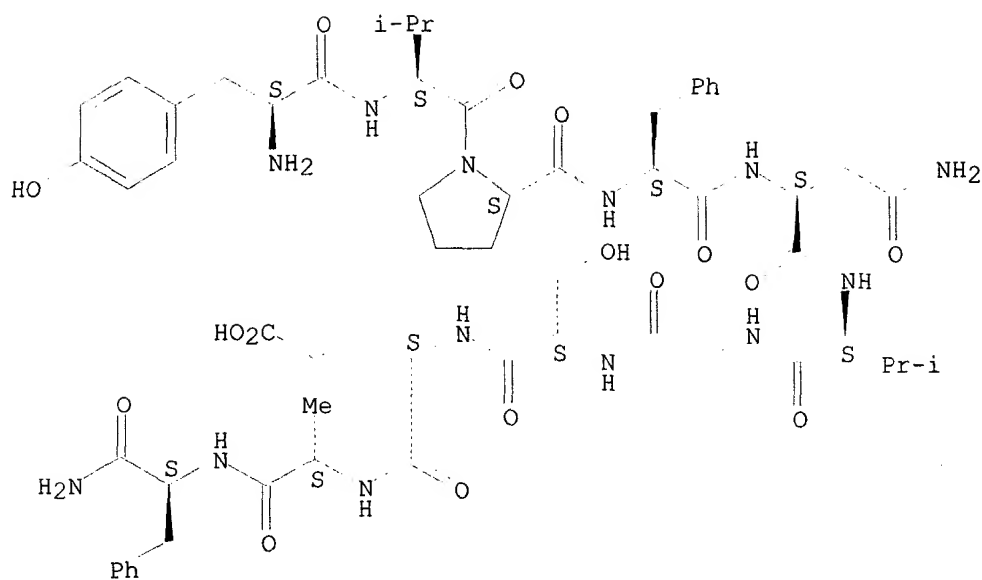


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NH₂

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Absolute stereochemistry.

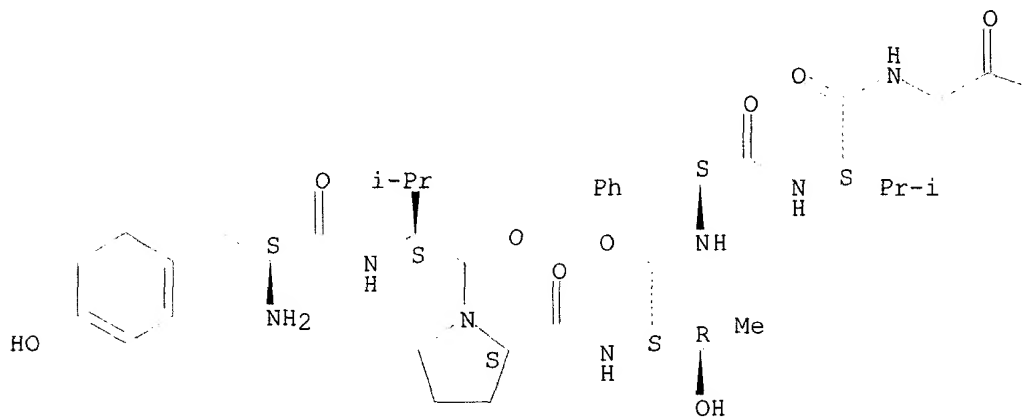


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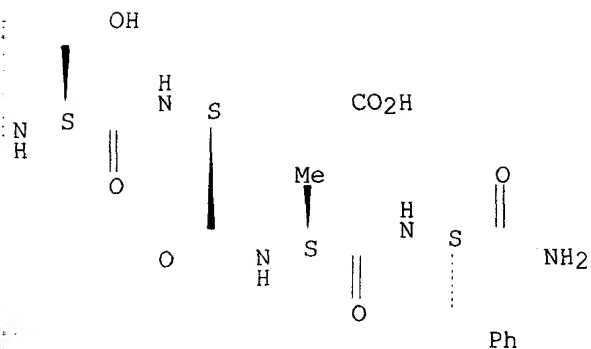
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Absolute stereochemistry.

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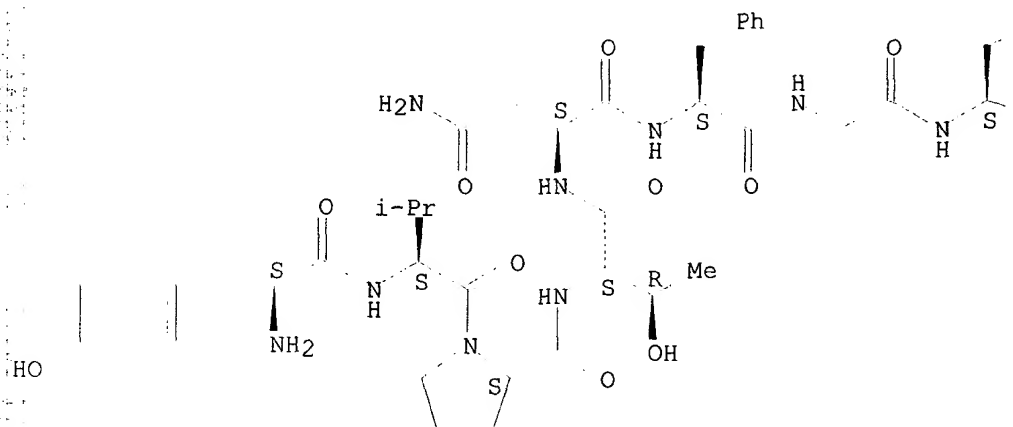


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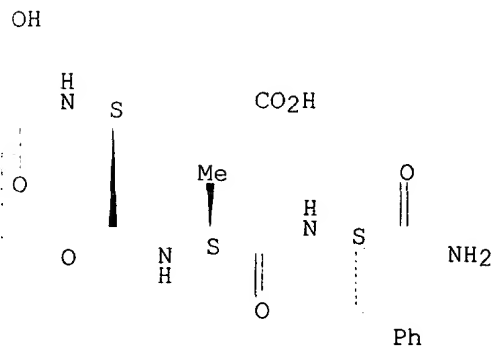
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Absolute stereochemistry.

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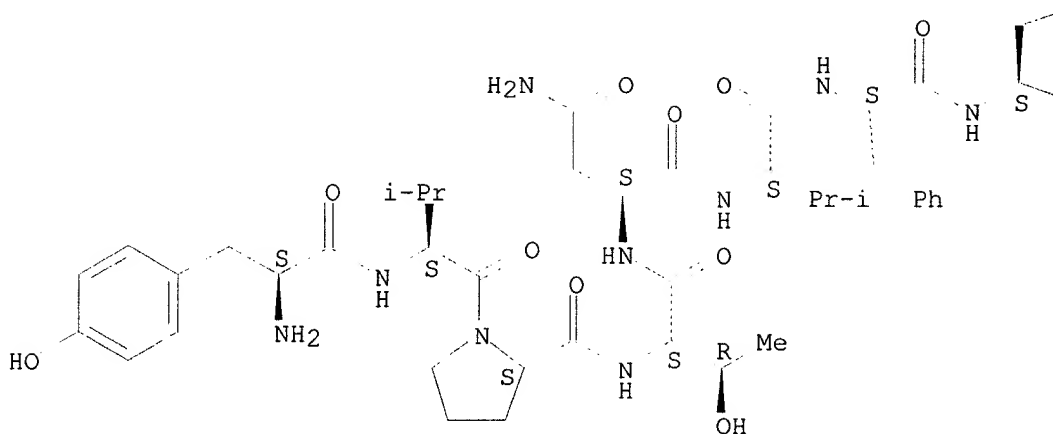


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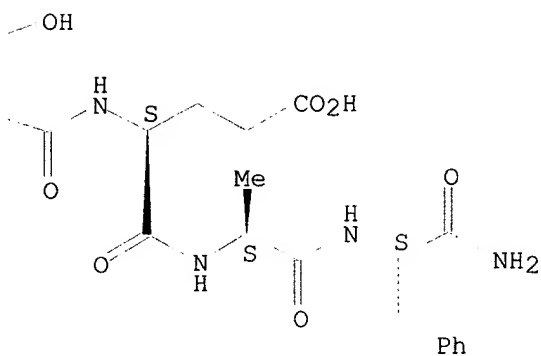
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Absolute stereochemistry.

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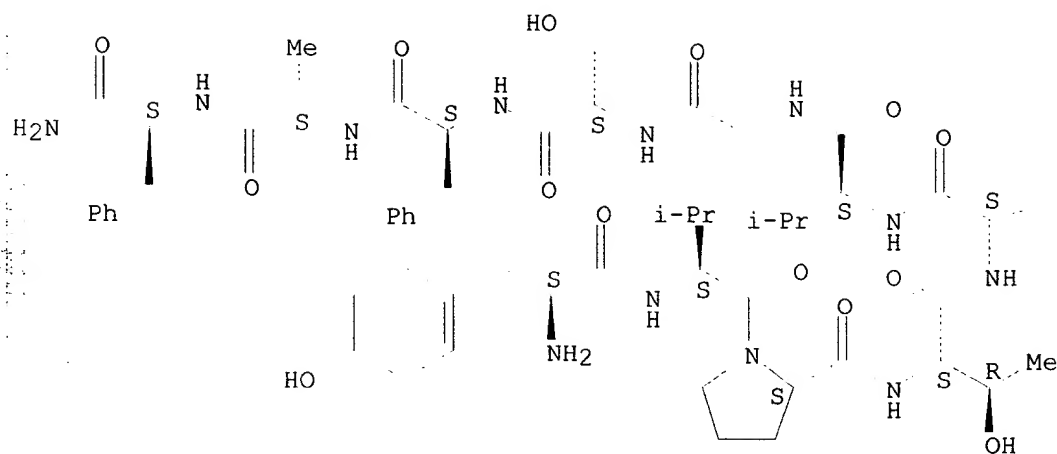


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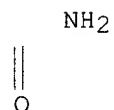
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Absolute stereochemistry.

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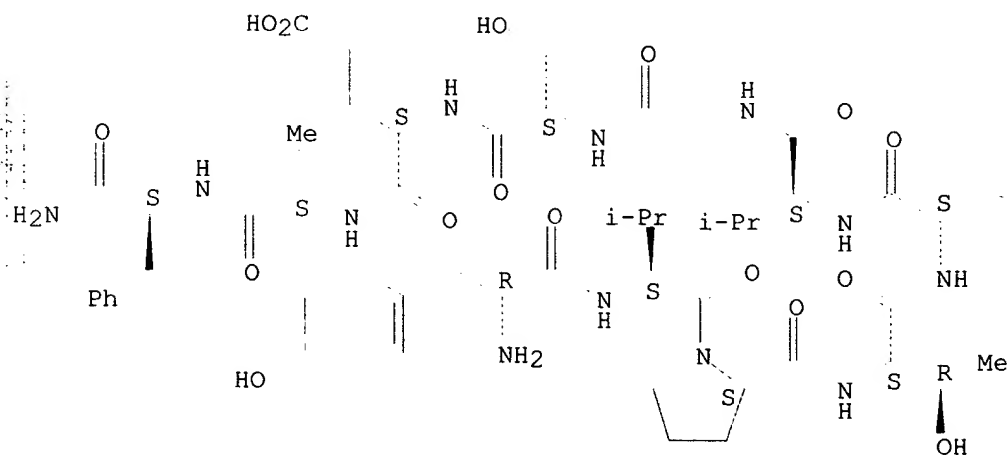
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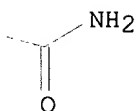
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Absolute stereochemistry.

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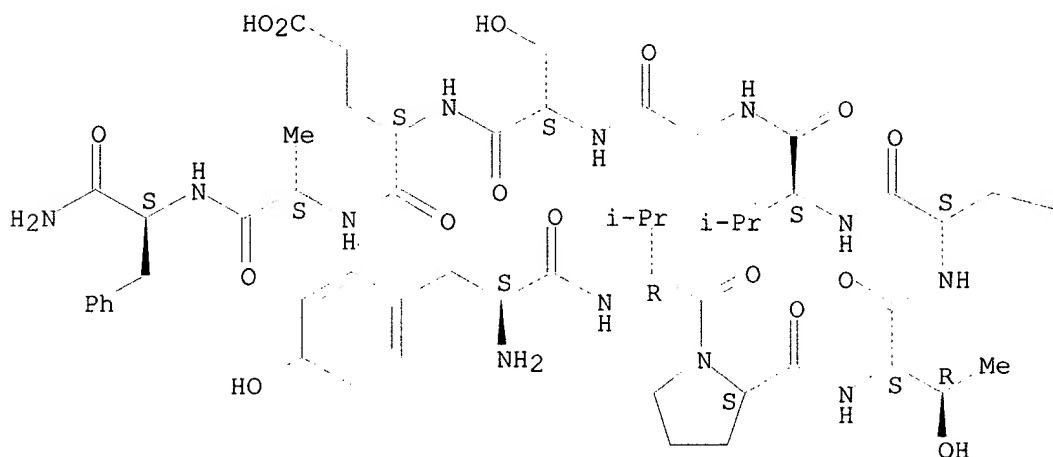


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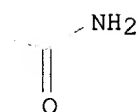
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Absolute stereochemistry.

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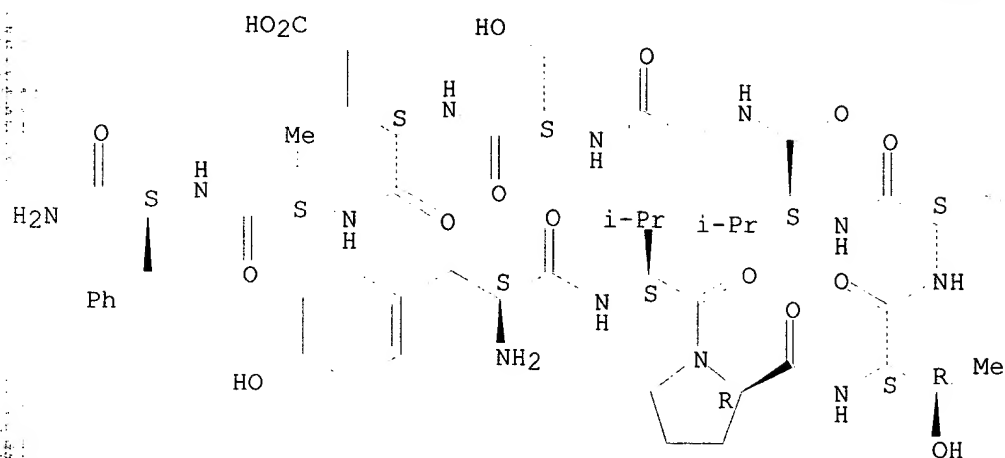
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Absolute stereochemistry.

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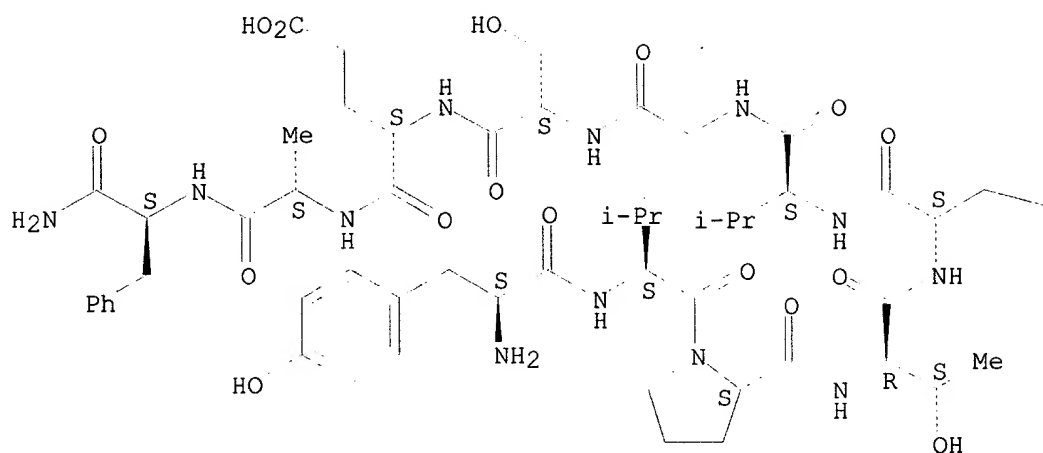
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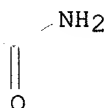
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Absolute stereochemistry.

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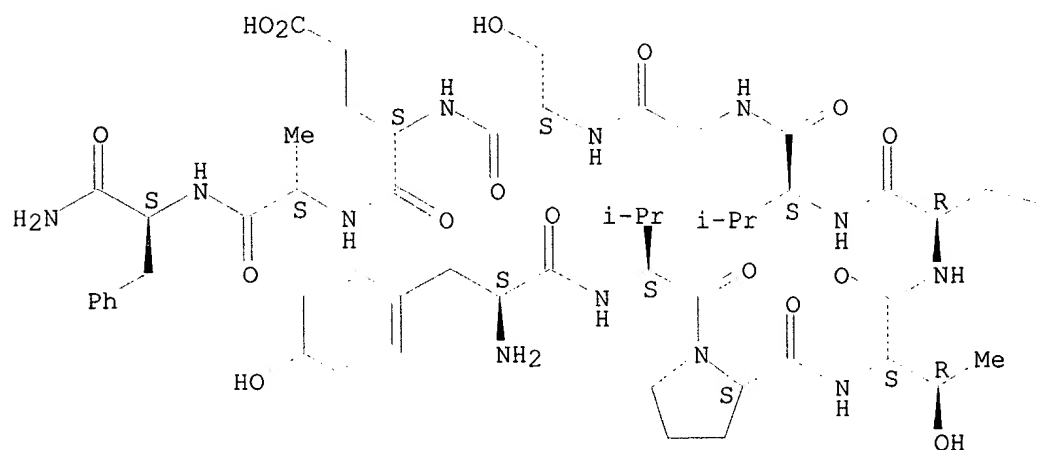
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RN 201613-16-3 CAPLUS
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Absolute stereochemistry.

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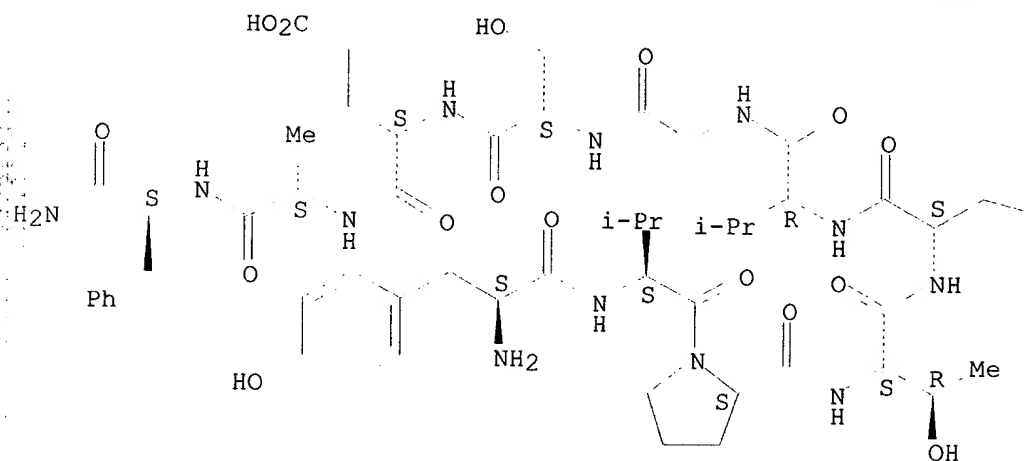
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NH₂

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Absolute stereochemistry.

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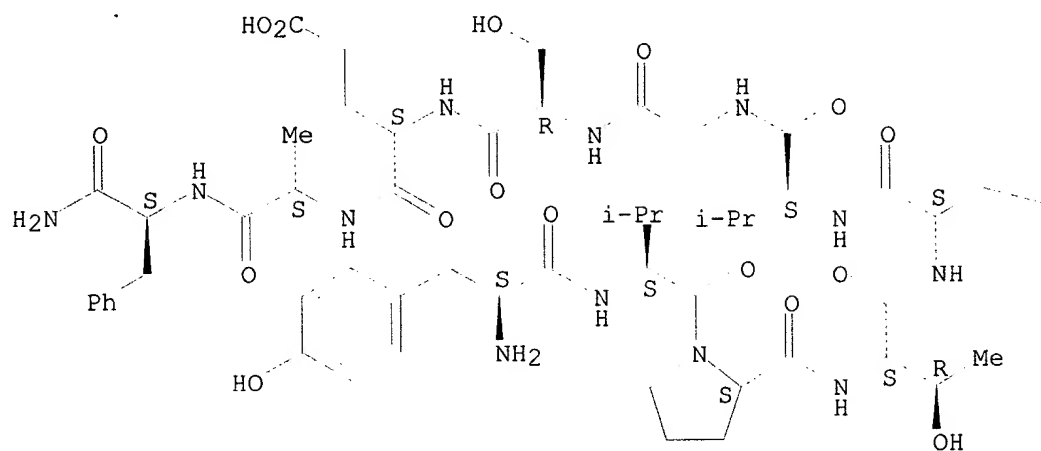
NH₂

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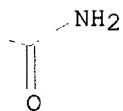
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Absolute stereochemistry.

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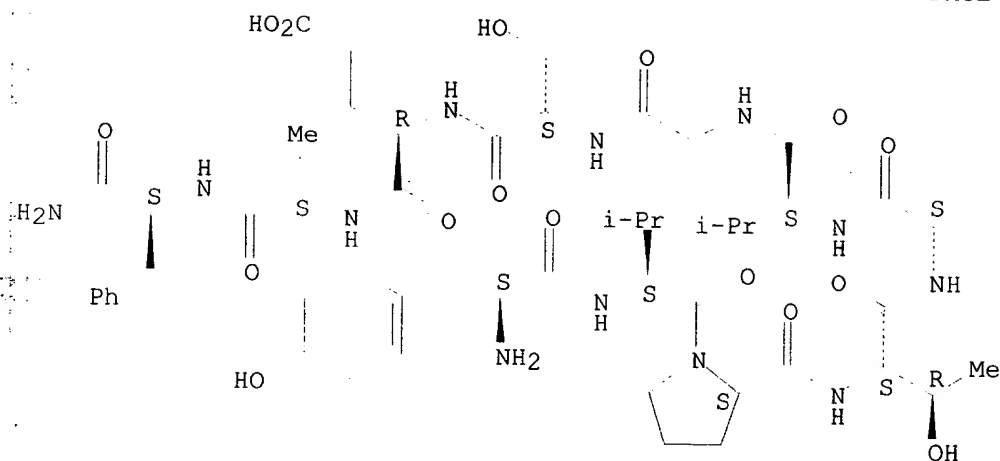
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CN L-Phenylalaninamide, L-tyrosyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyll-L-valylglycyl-L-seryl-D-.alpha.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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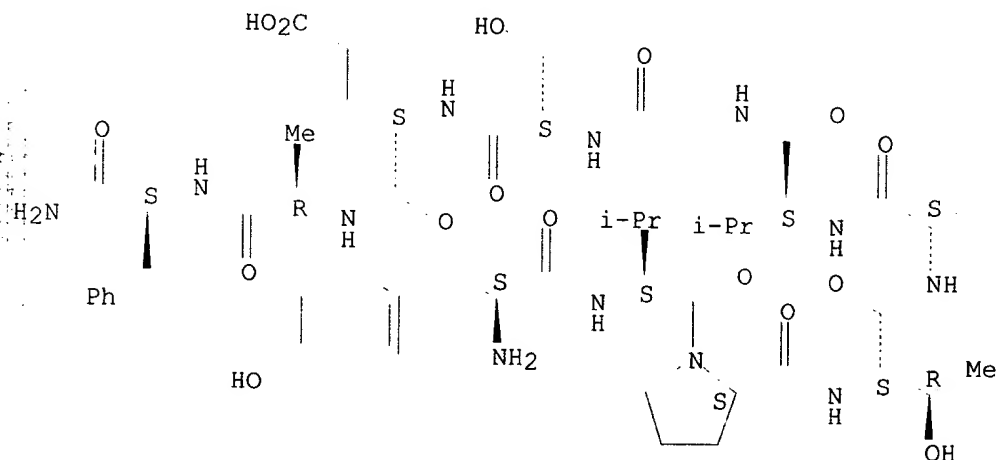
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NH₂

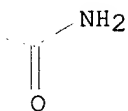
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Absolute stereochemistry.

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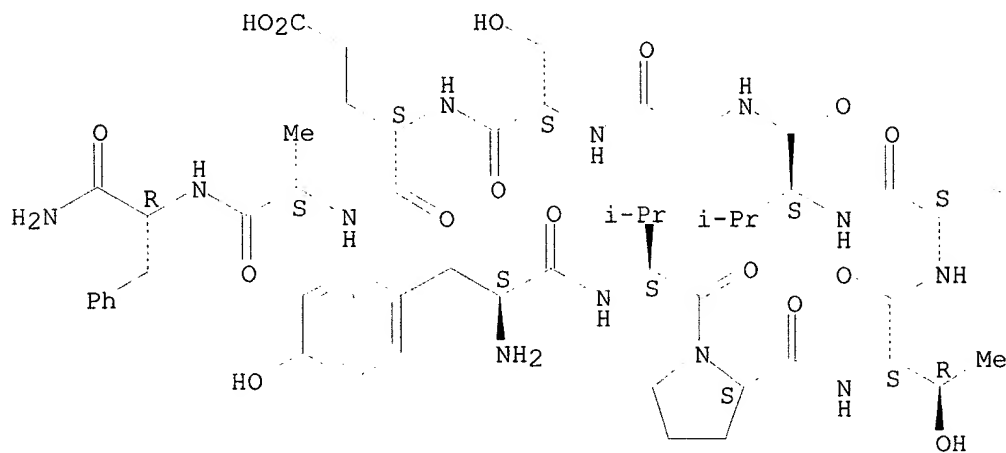
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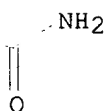
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Absolute stereochemistry.

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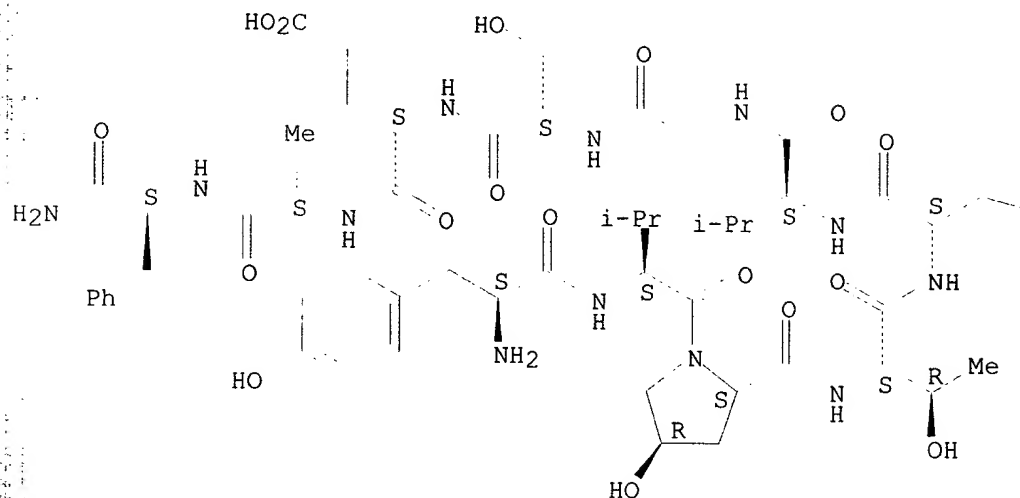


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(CA INDEX NAME)

Absolute stereochemistry.

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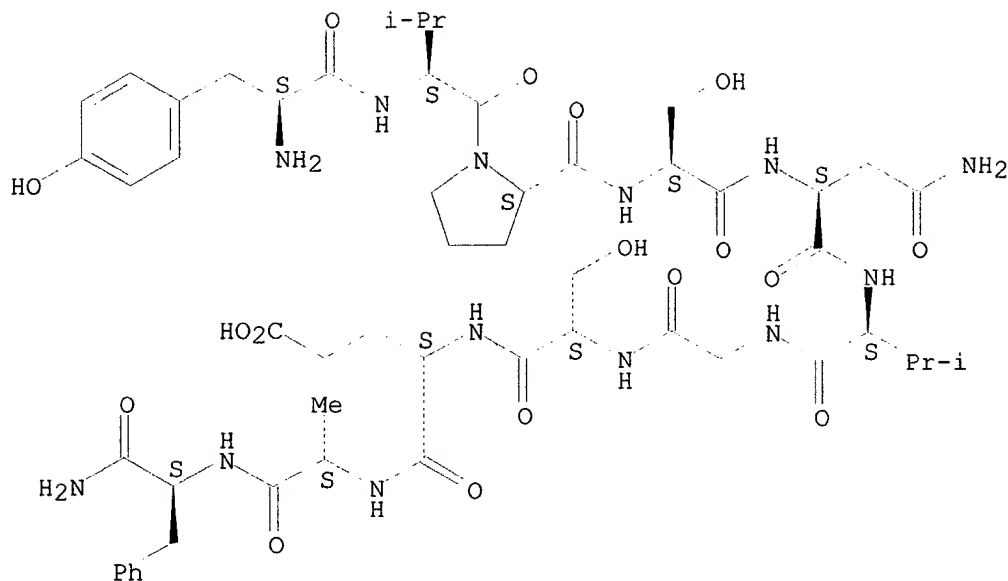


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NH₂

RN 201613-23-2 CAPLUS
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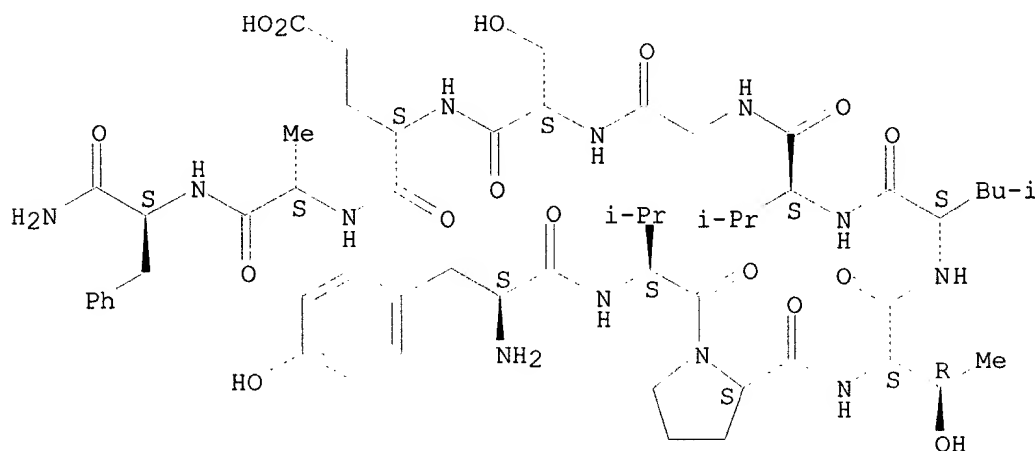
Absolute stereochemistry.



RN 201613-24-3 CAPLUS

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Absolute stereochemistry.

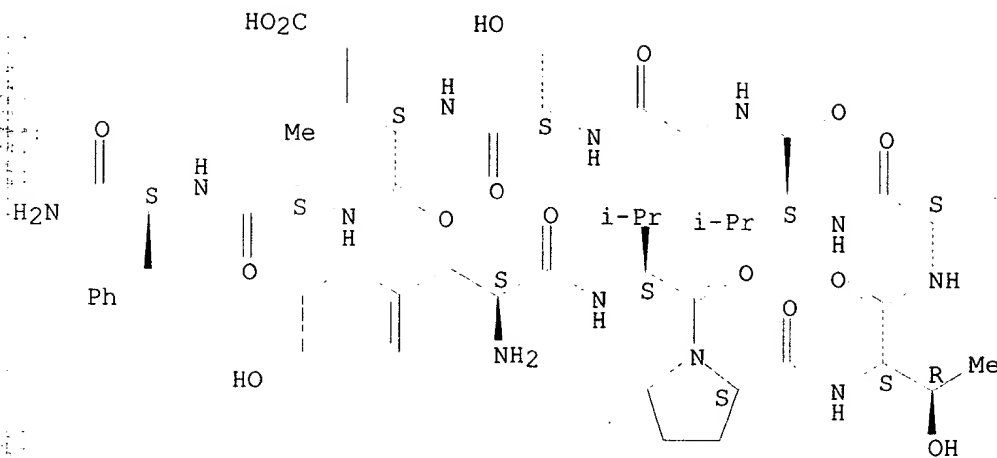


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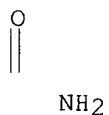
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Absolute stereochemistry.

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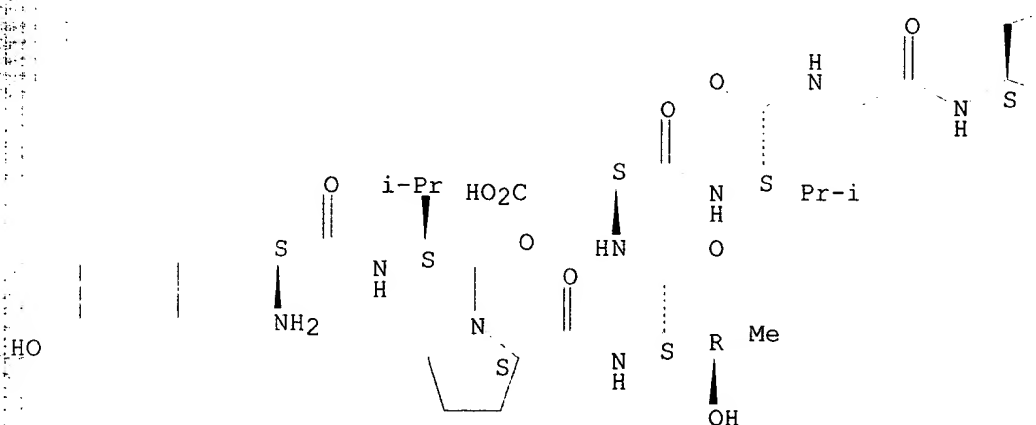
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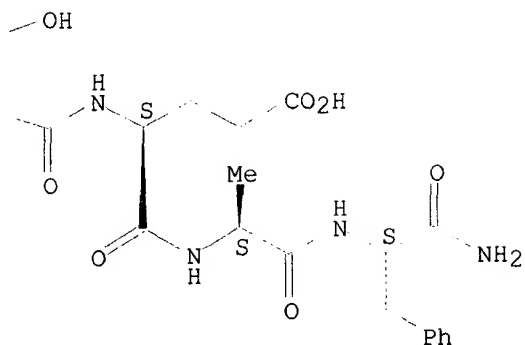
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 INDEX NAME)

Absolute stereochemistry.

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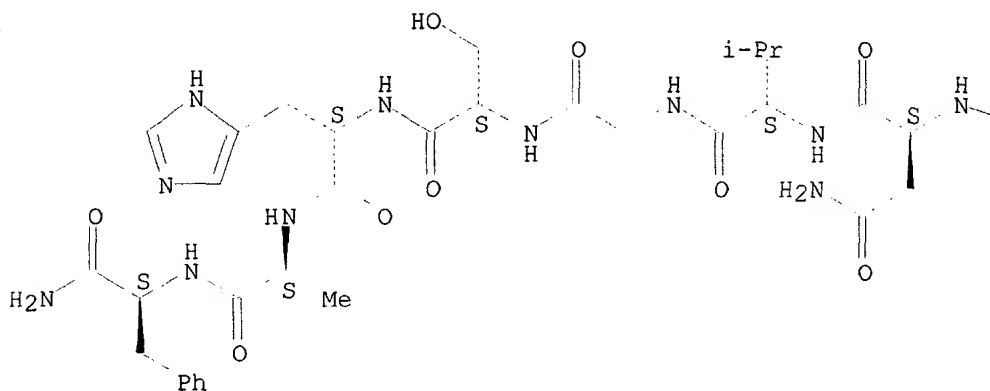


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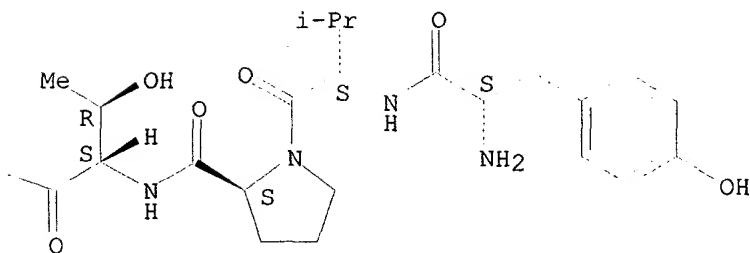
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Absolute stereochemistry.

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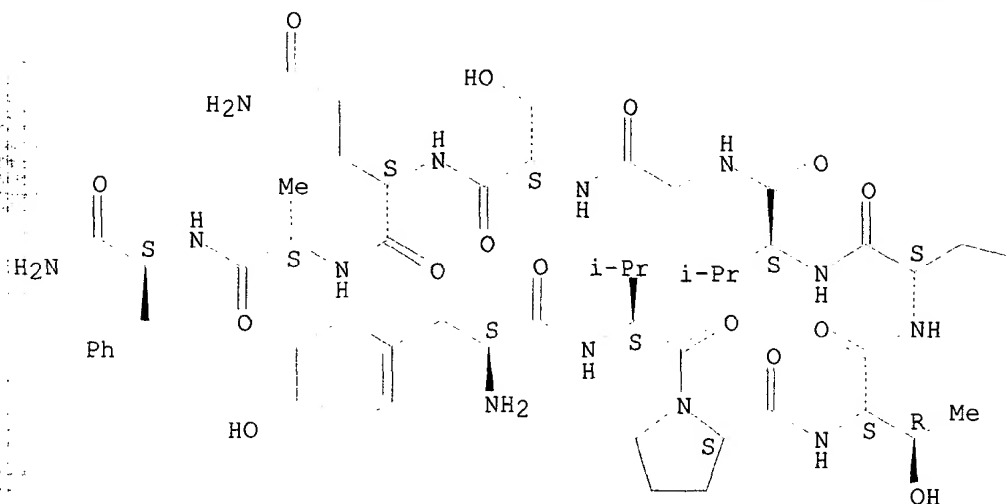
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valylglycyl-L-seryl-L-glutaminyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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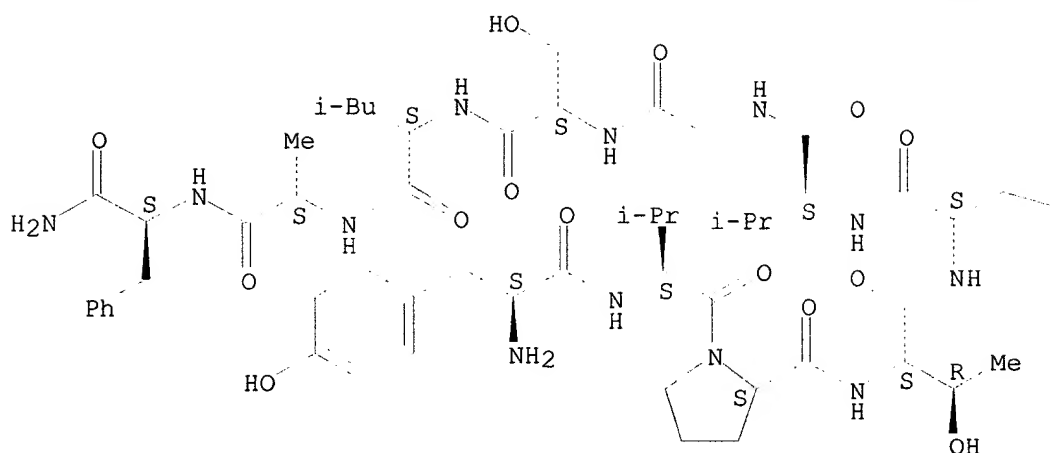


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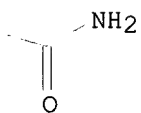
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Absolute stereochemistry.

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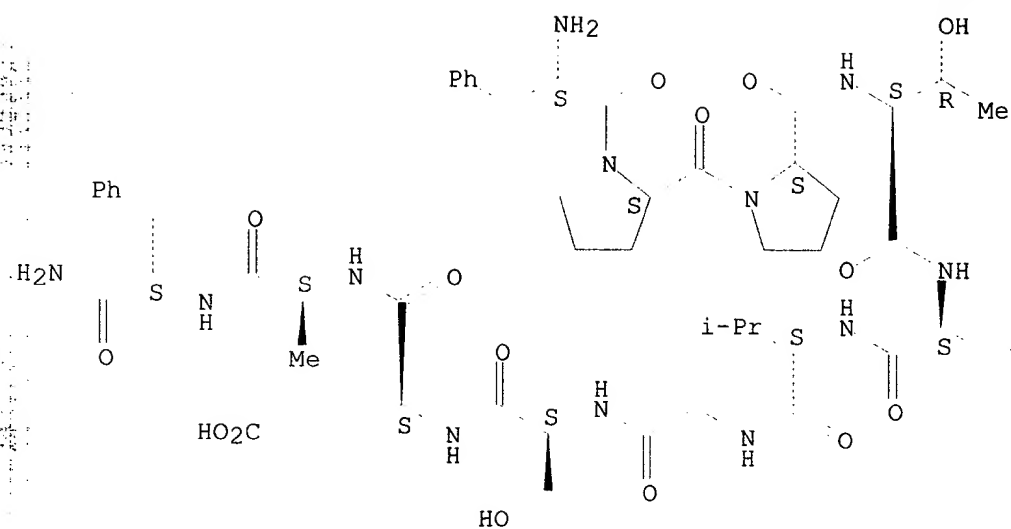
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RN 201613-32-3 CAPLUS
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Absolute stereochemistry.

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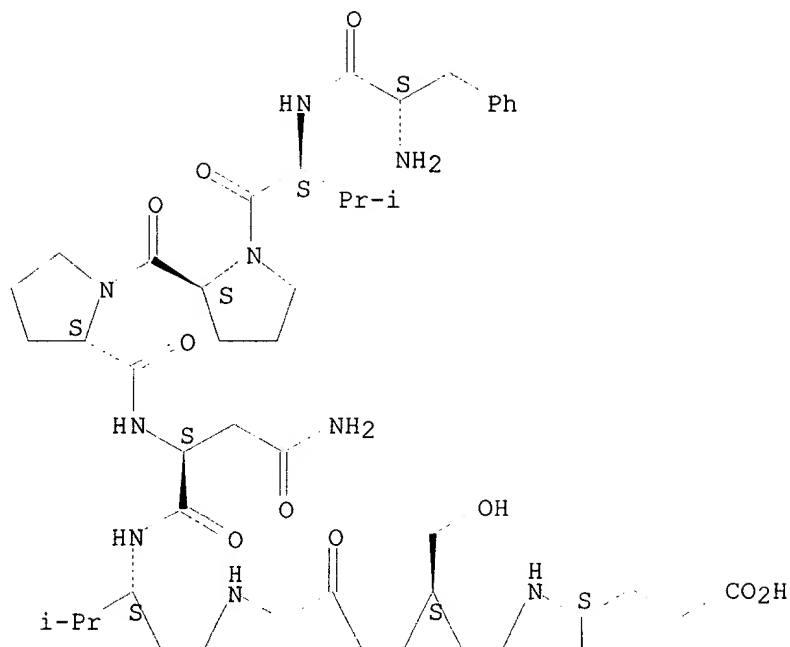
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NH₂

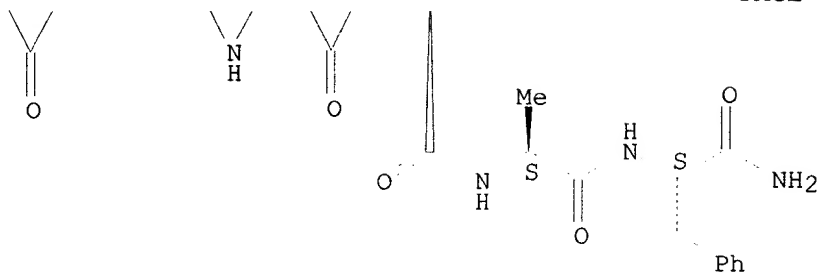
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Absolute stereochemistry.

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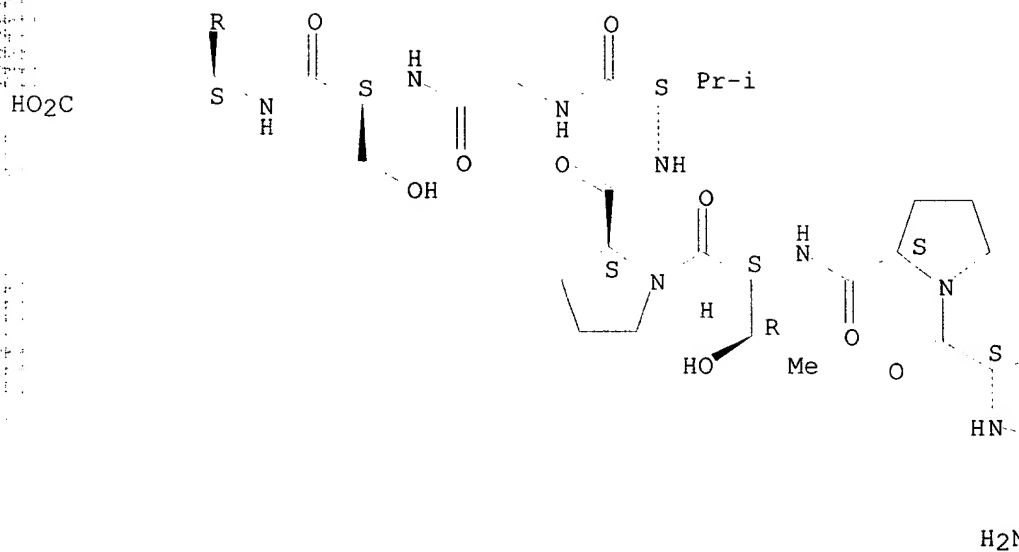


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CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-prolyl-L-valylglycyl-L-seryl-L-.alpha.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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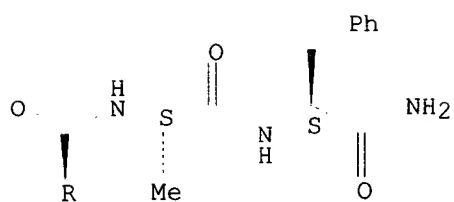
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PAGE 2-A

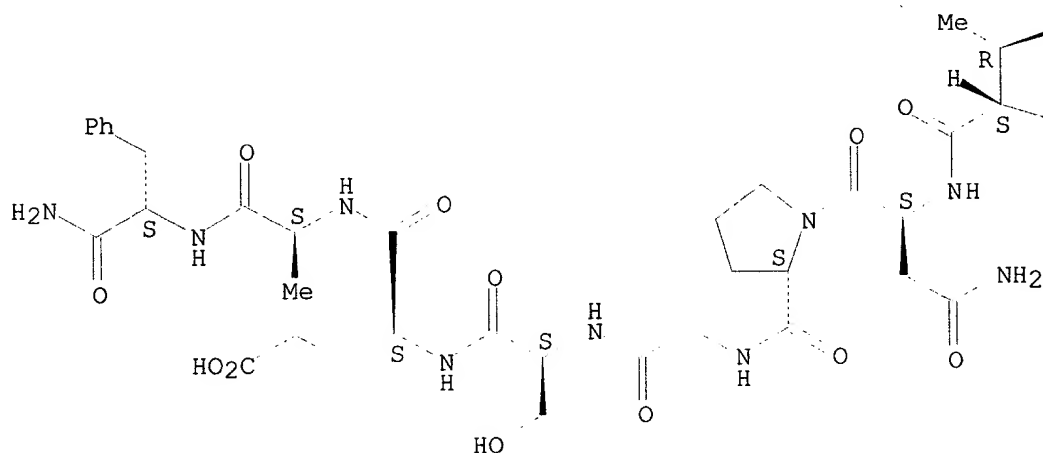


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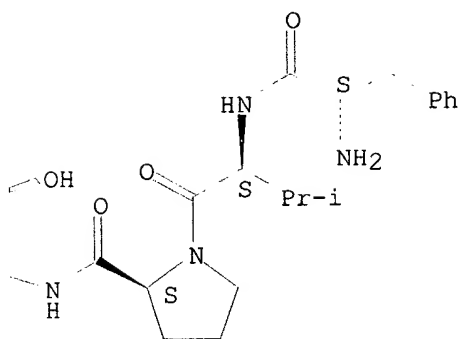
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Absolute stereochemistry.

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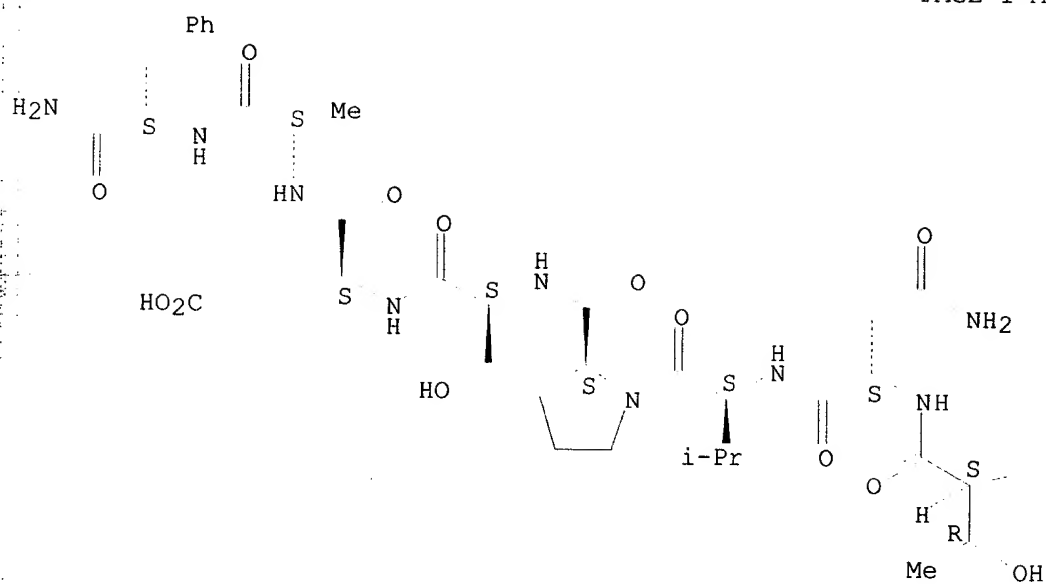


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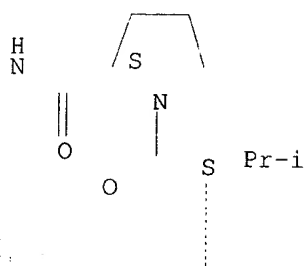
CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valyl-L-prolyl-L-seryl-L-.alpha.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

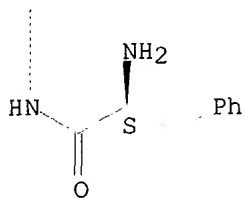
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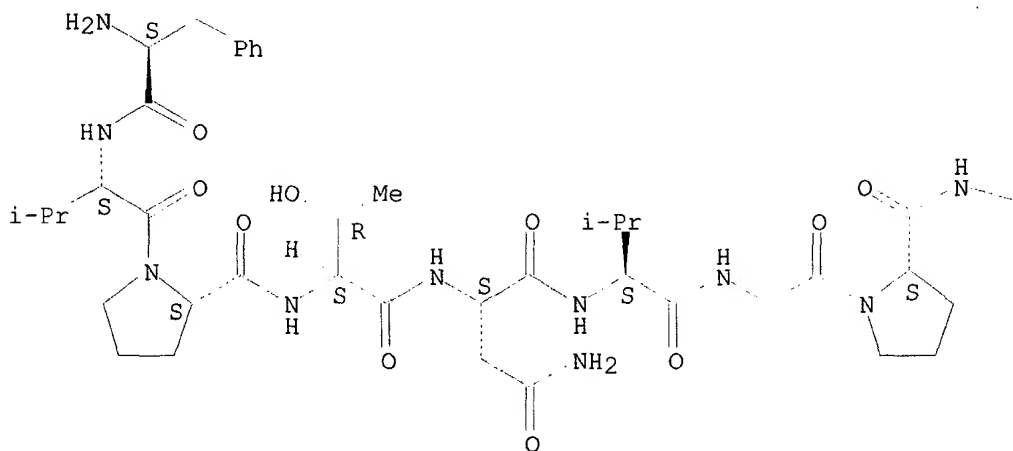


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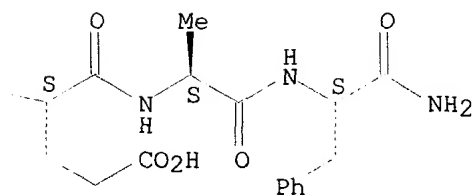
CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-prolyl-L-.alpha.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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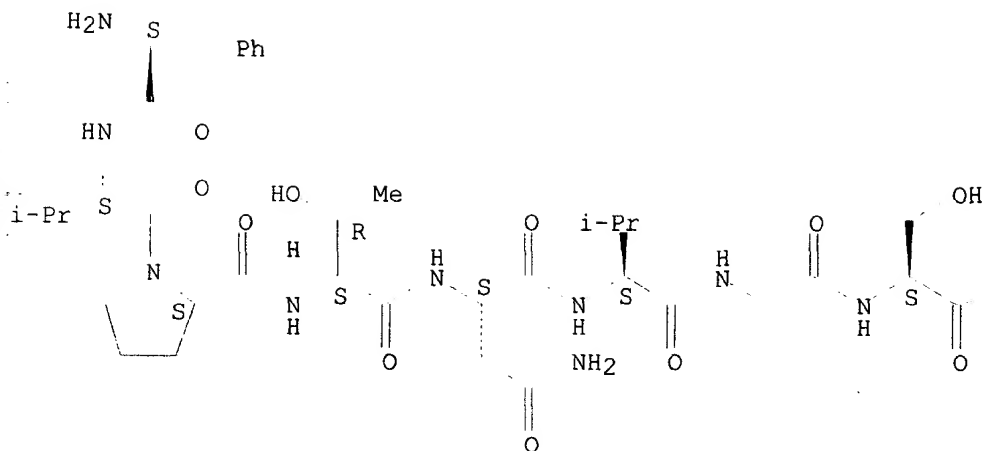


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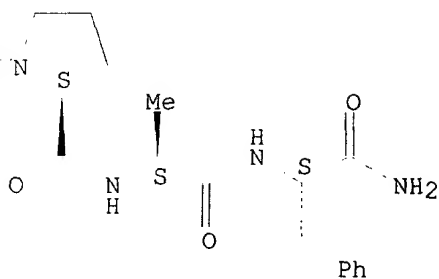
CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-prolyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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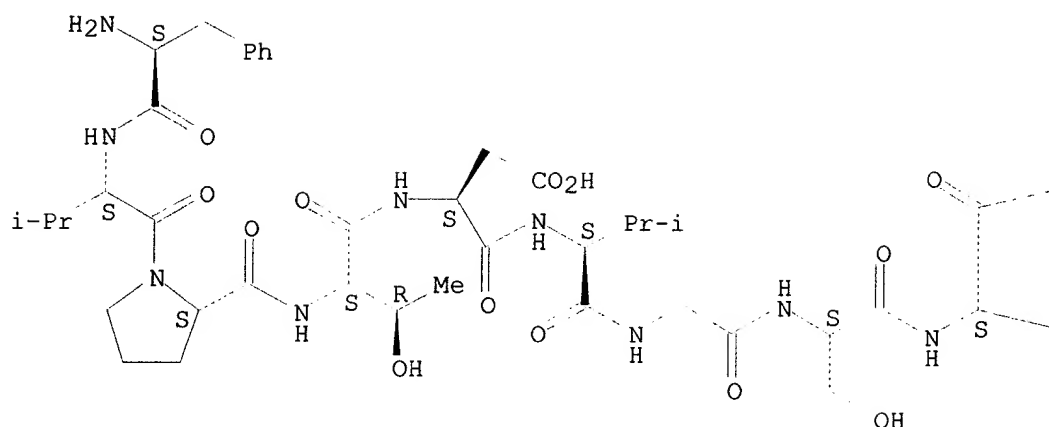


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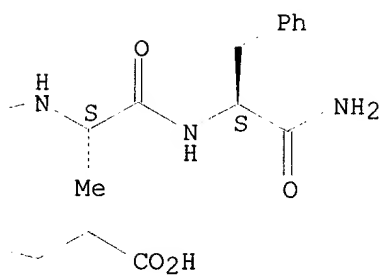
CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
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 INDEX NAME)

Absolute stereochemistry.

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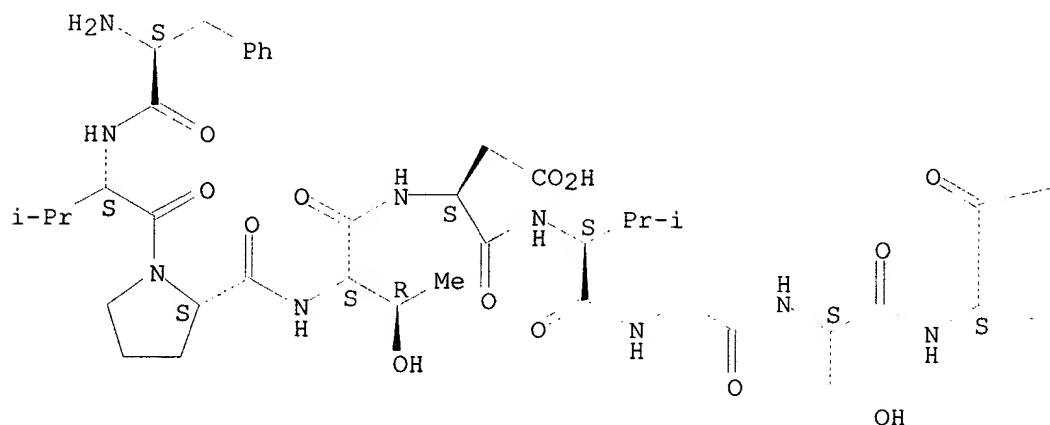
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RN 201613-42-5 CAPLUS
 CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
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 NAME)

Absolute stereochemistry.

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Absolute stereochemistry.

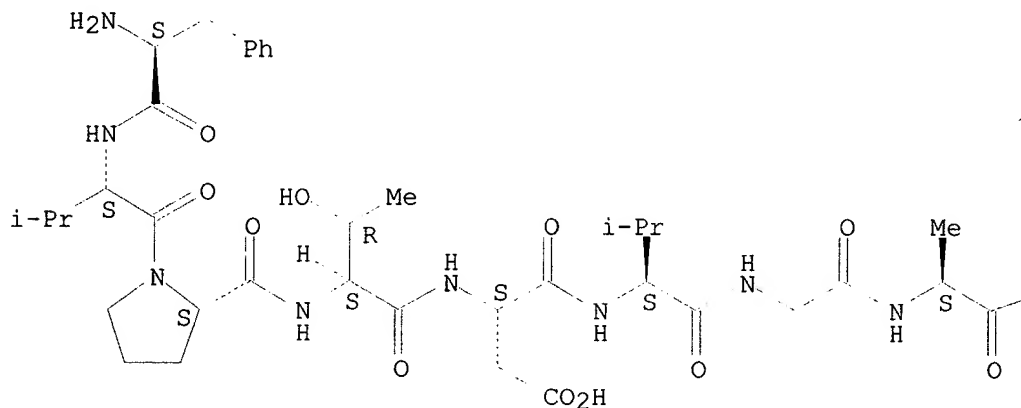
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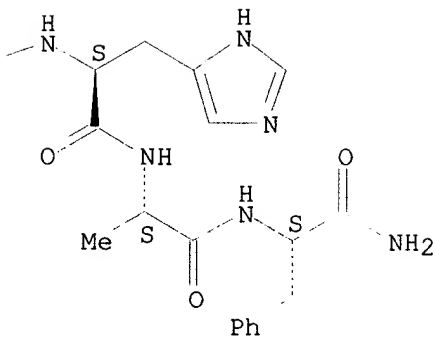
CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
aspartyl-L-valylglycyl-L-alanyl-L-histidyl-L-alanyl- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

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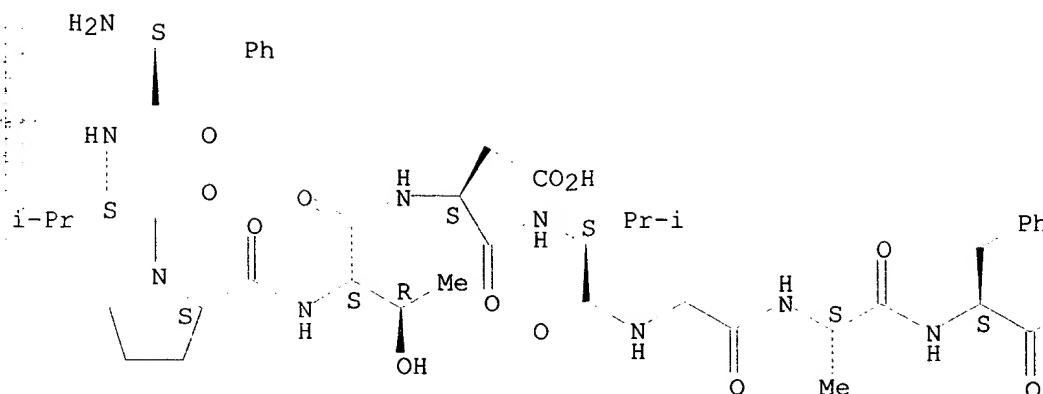


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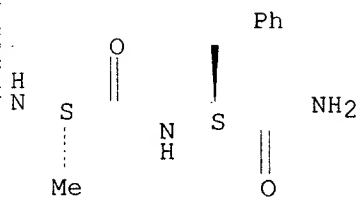
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NAME)

Absolute stereochemistry.

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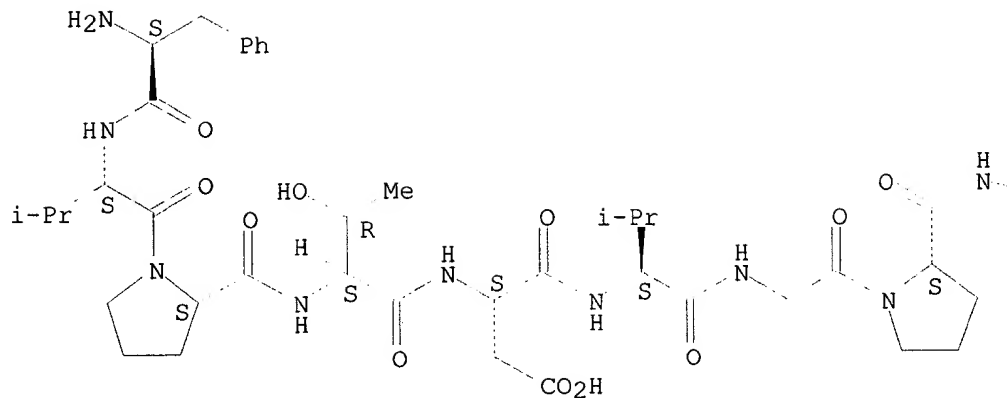
PAGE 1-B



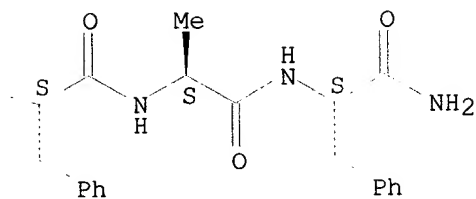
RN 201613-51-6 CAPLUS
CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
aspartyl-L-valylglycyl-L-prolyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

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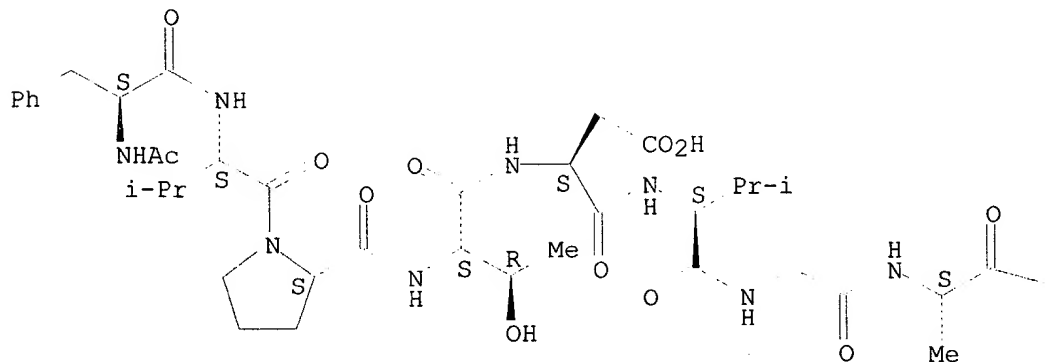
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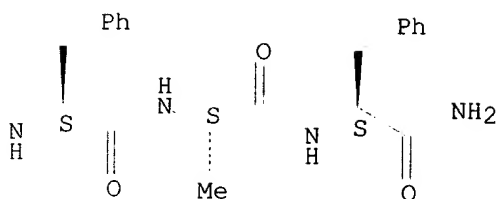
RN 201613-53-8 CAPLUS
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 (CA INDEX NAME)

Absolute stereochemistry.

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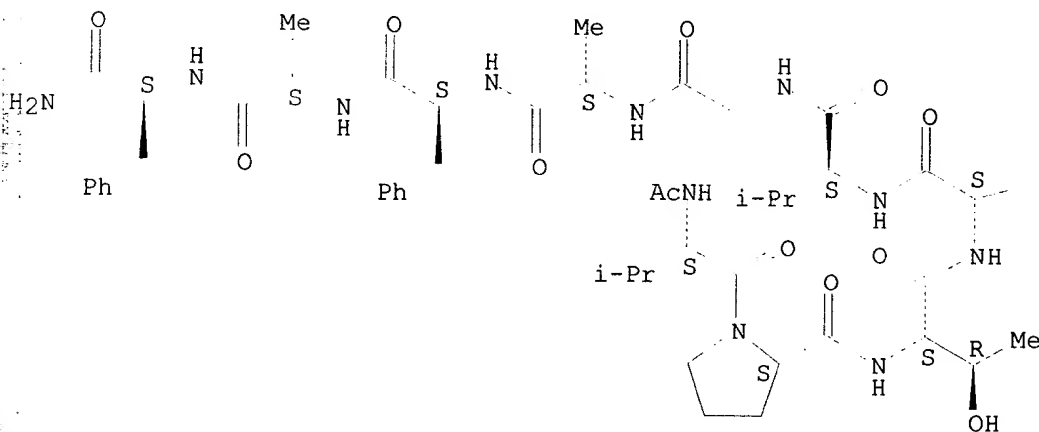
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L-Phenylalaninamide, N-acetyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
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NAME)

Absolute stereochemistry.

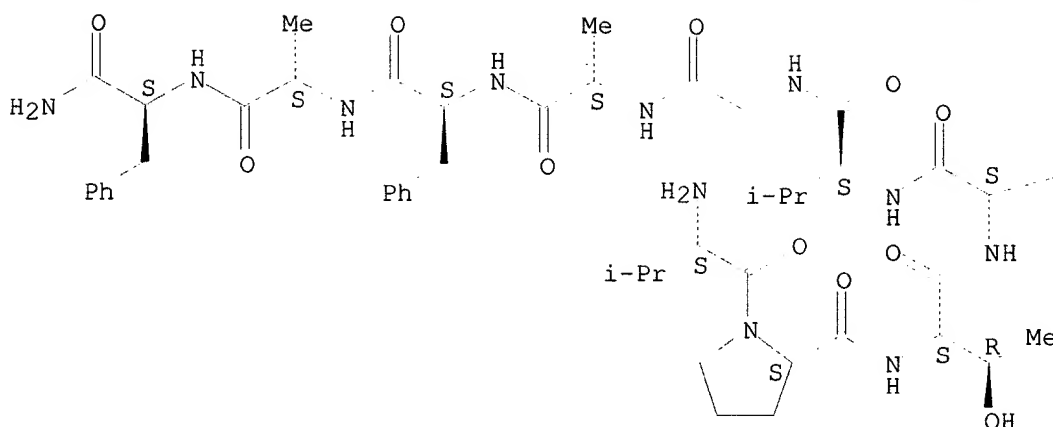
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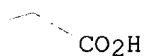
L-Phenylalaninamide, L-valyl-L-prolyl-L-threonyl-L-.alpha.-aspartyl-L-valylglycyl-L-alanyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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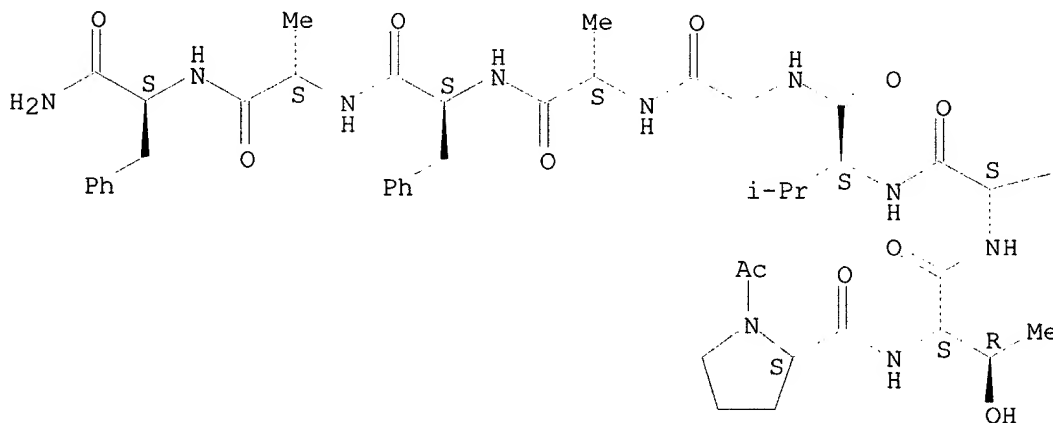


RN 201613-59-4 CAPLUS

CN L-Phenylalaninamide, 1-acetyl-L-prolyl-L-threonyl-L-.alpha.-aspartyl-L-valylglycyl-L-alanyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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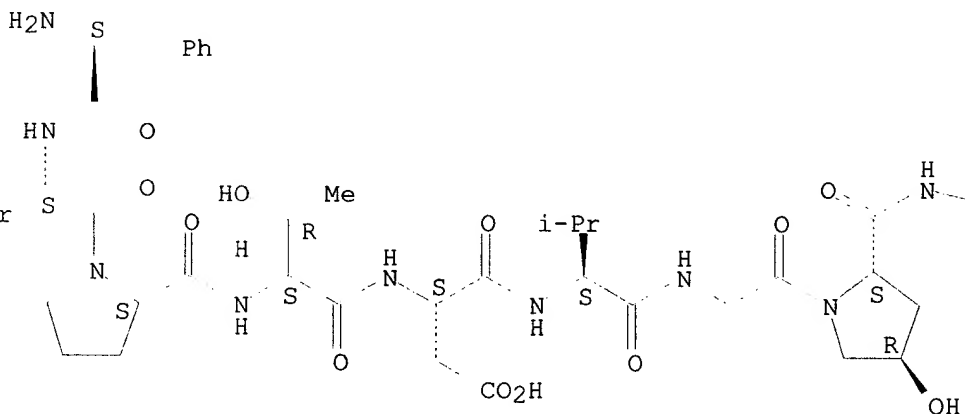
PAGE 1-B

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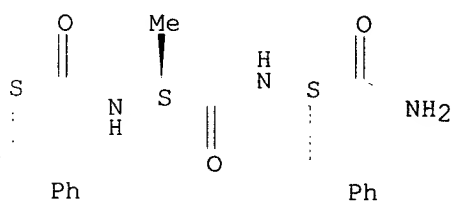
RN 201613-71-0 CAPLUS
CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
aspartyl-L-valylglycyl-(4R)-4-hydroxy-L-prolyl-L-phenylalanyl-L-alanyl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

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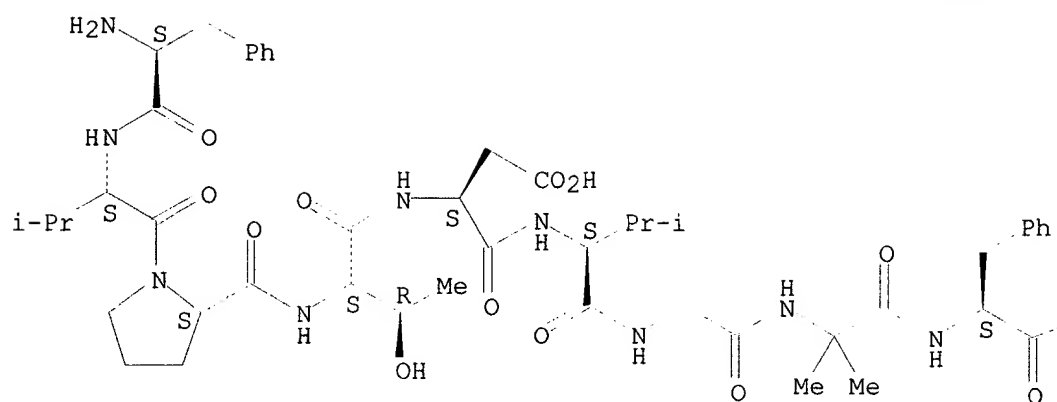
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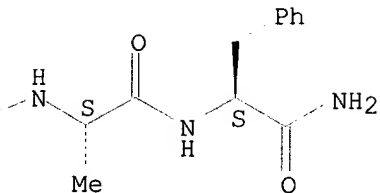
RN 201613-75-4 CAPLUS
CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
aspartyl-L-valylglycyl-2-methylalanyl-L-phenylalanyl-L-alanyl- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

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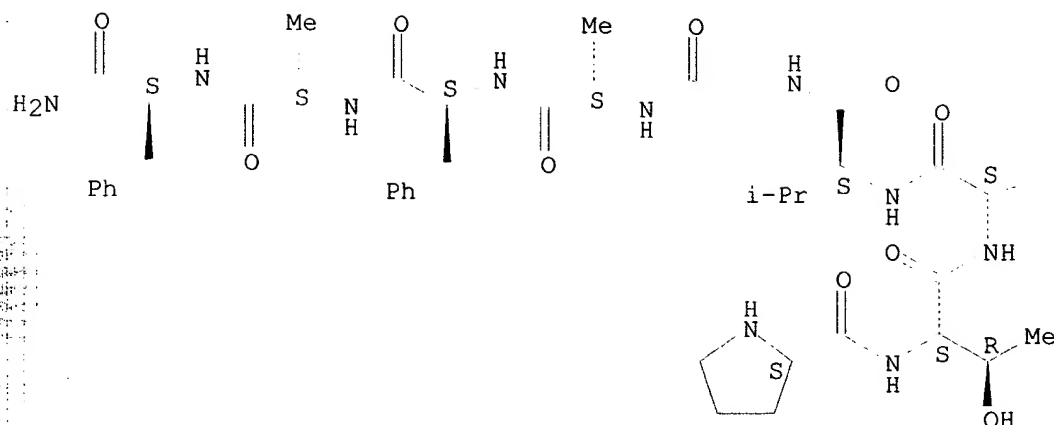


RN 201613-76-5 CAPLUS

CN L-Phenylalaninamide, L-prolyl-L-threonyl-L-.alpha.-aspartyl-L-valylglycyl-L-alanyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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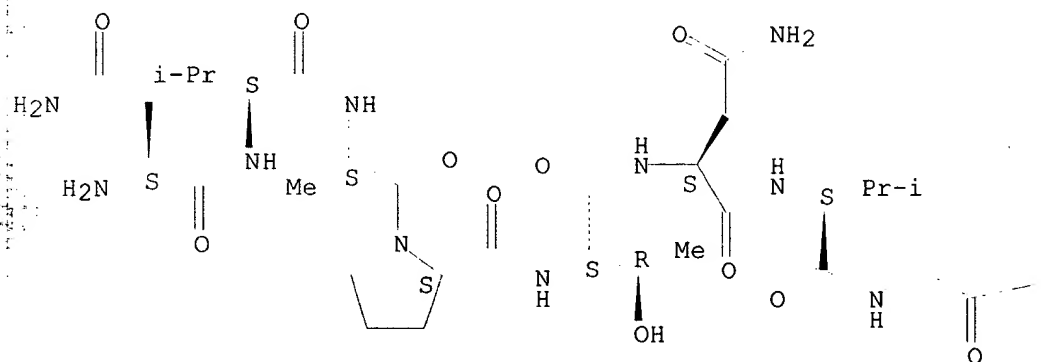
PAGE 1-B

CO₂H

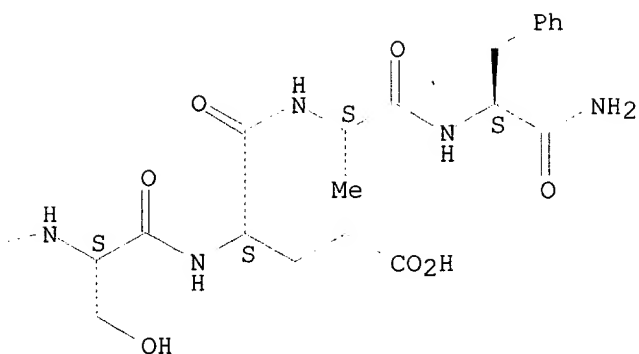
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Absolute stereochemistry.

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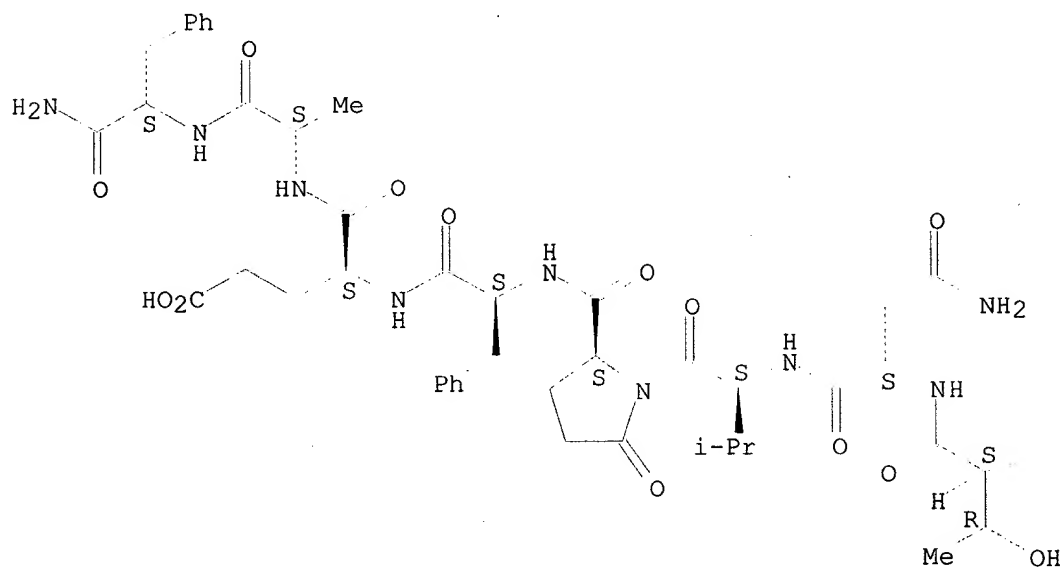


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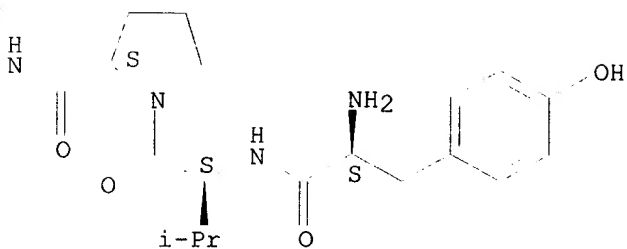
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(CA INDEX NAME)

Absolute stereochemistry.

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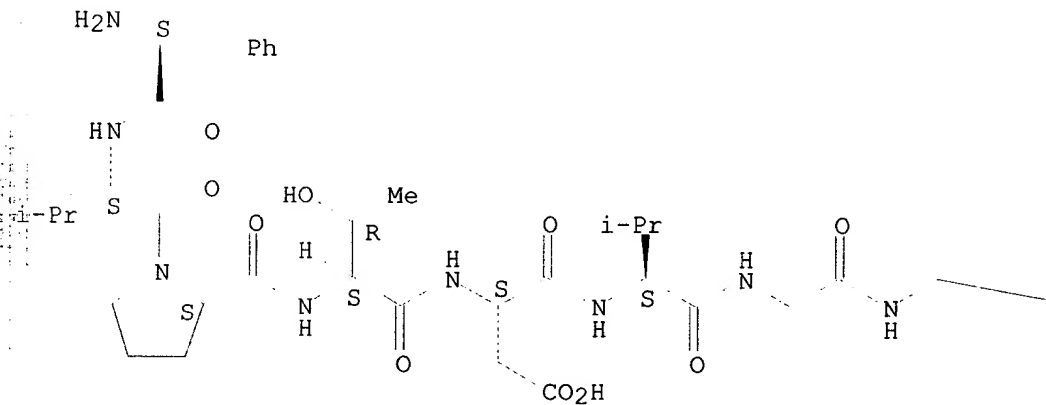
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RN 220198-69-6 CAPLUS
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L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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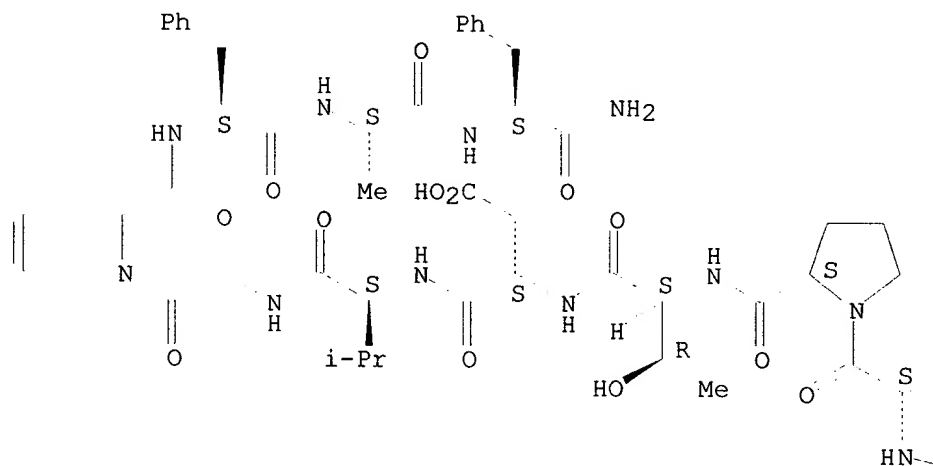
Absolute stereochemistry.

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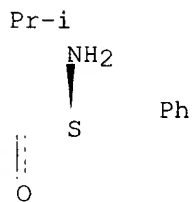
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CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
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phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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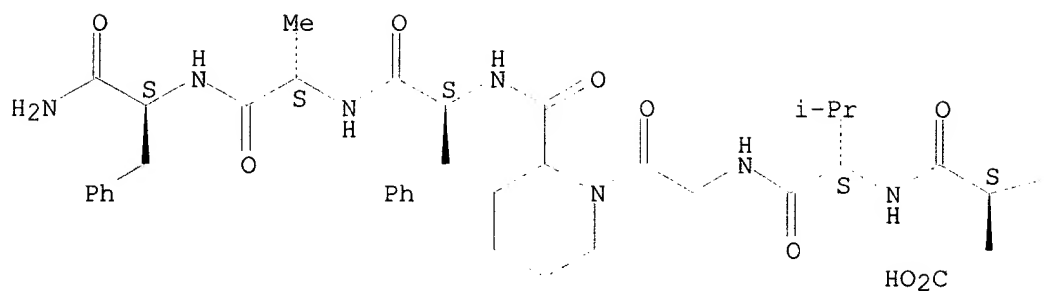
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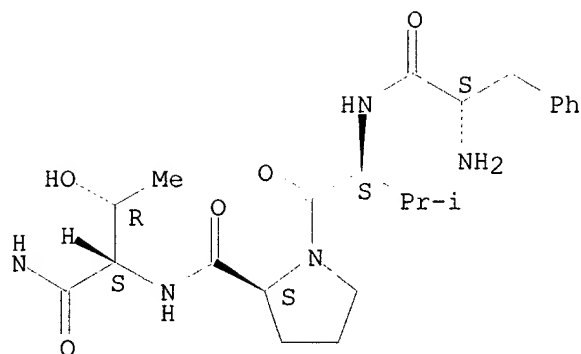
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CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-.alpha.-
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(CA INDEX NAME)

Absolute stereochemistry.

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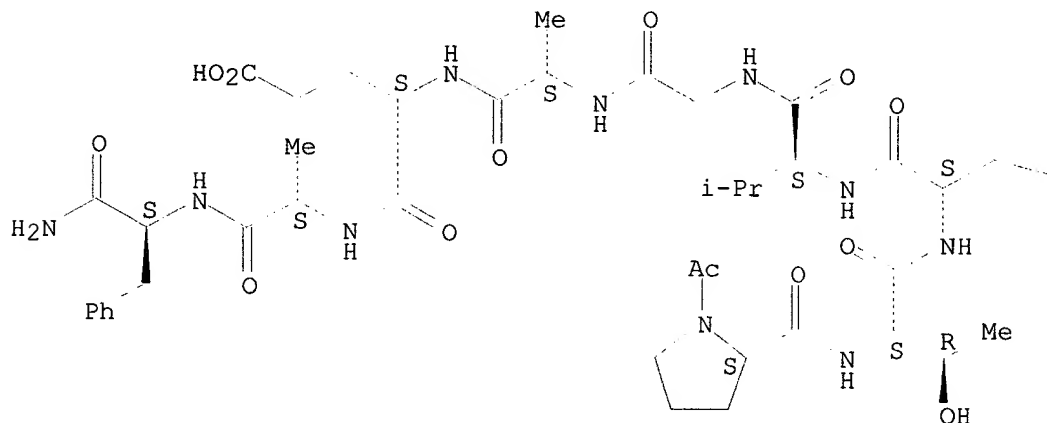
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RN 220198-76-5 CAPLUS
CN L-Phenylalaninamide, 1-acetyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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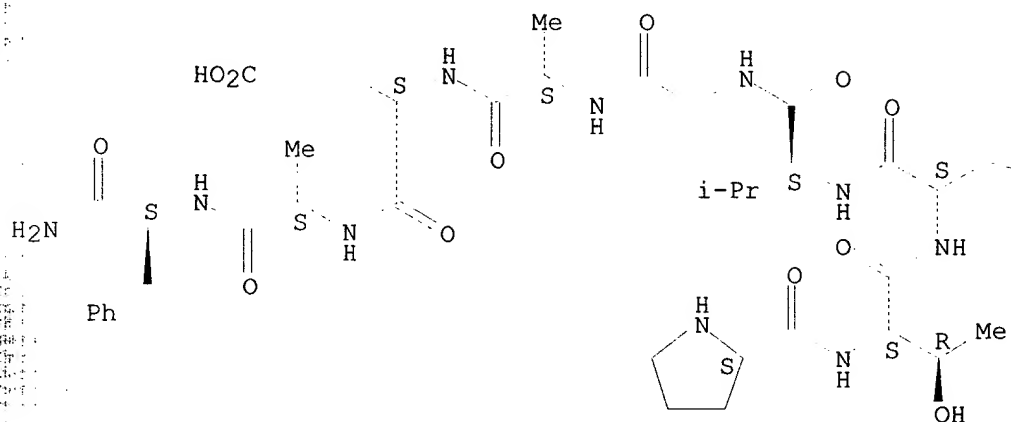
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NH₂

RN 220198-77-6 CAPLUS
CN L-Phenylalaninamide, L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-alanyl-L-.alpha.-glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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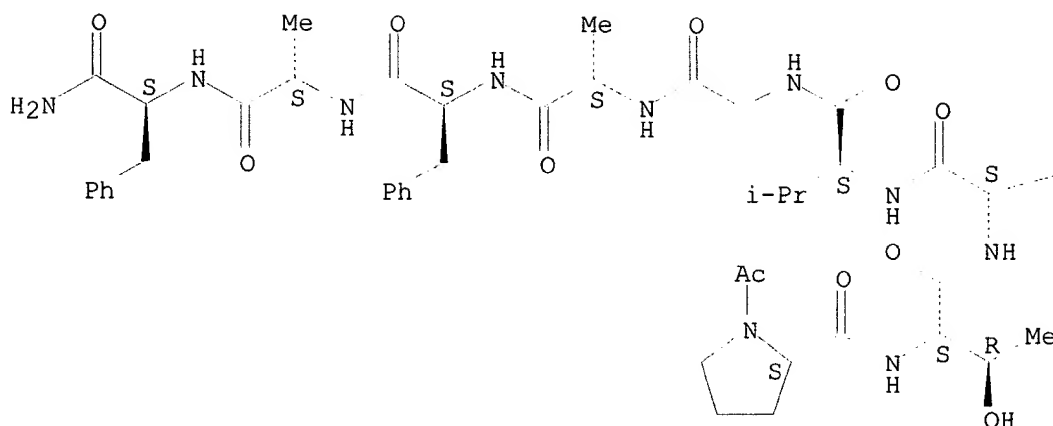
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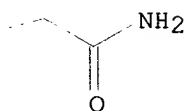
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Absolute stereochemistry.

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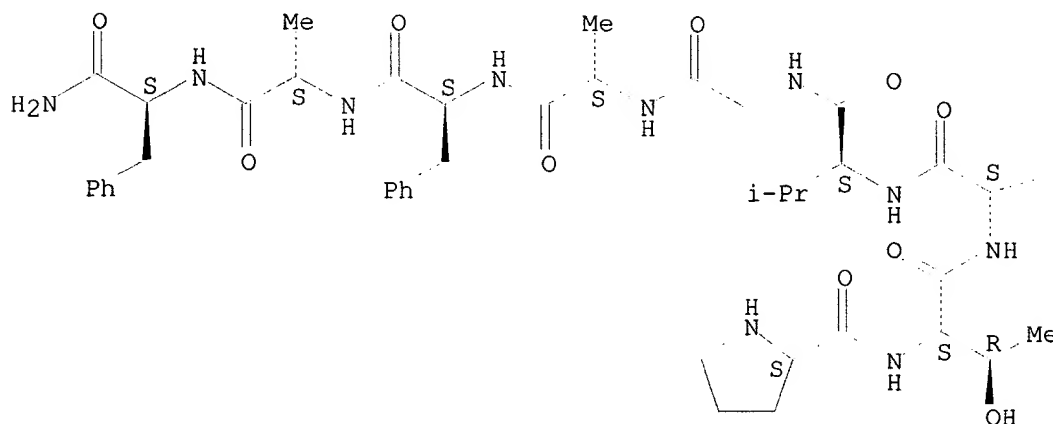


RN 220198-79-8 CAPLUS

CN L-Phenylalaninamide, L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-alanyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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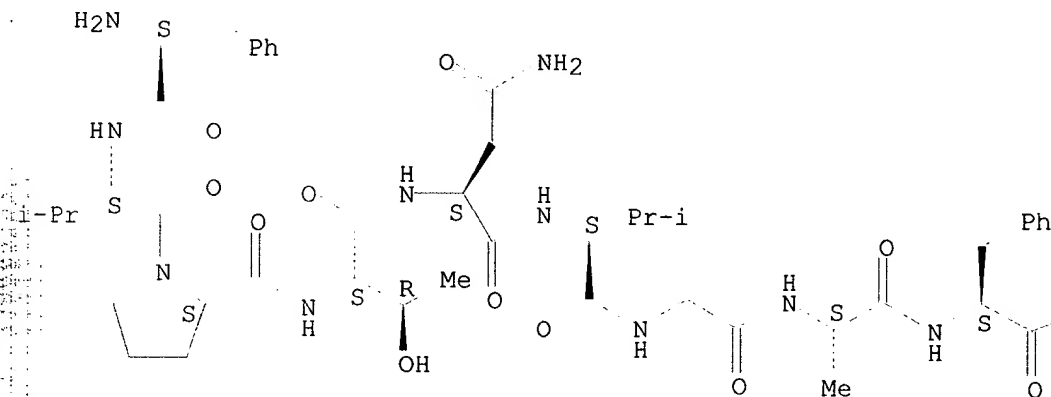
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NH₂

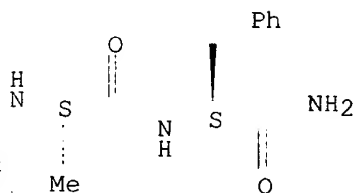
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Absolute stereochemistry.

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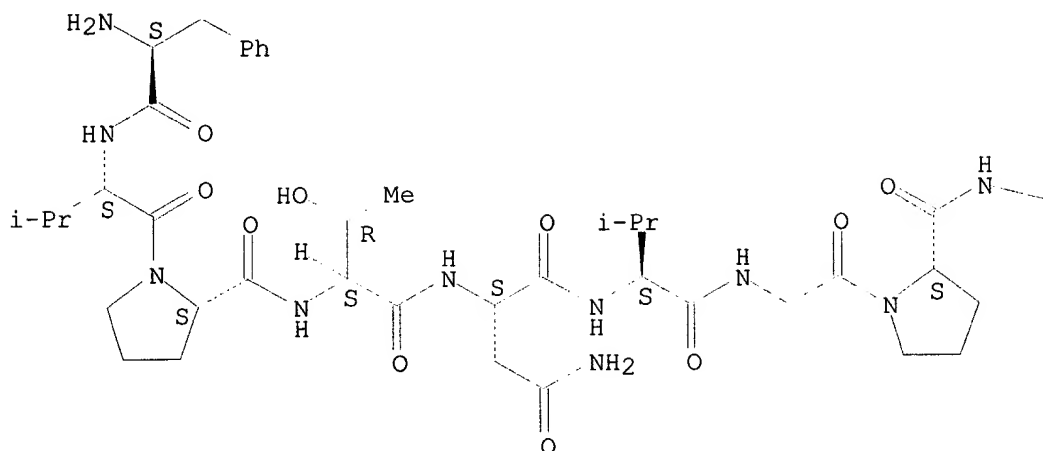


RN 220198-81-2 CAPLUS
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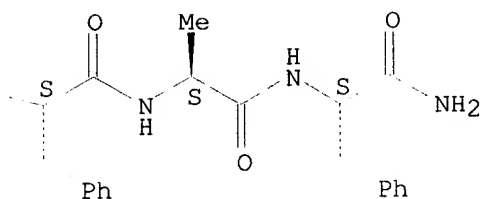
INDEX NAME)

Absolute stereochemistry.

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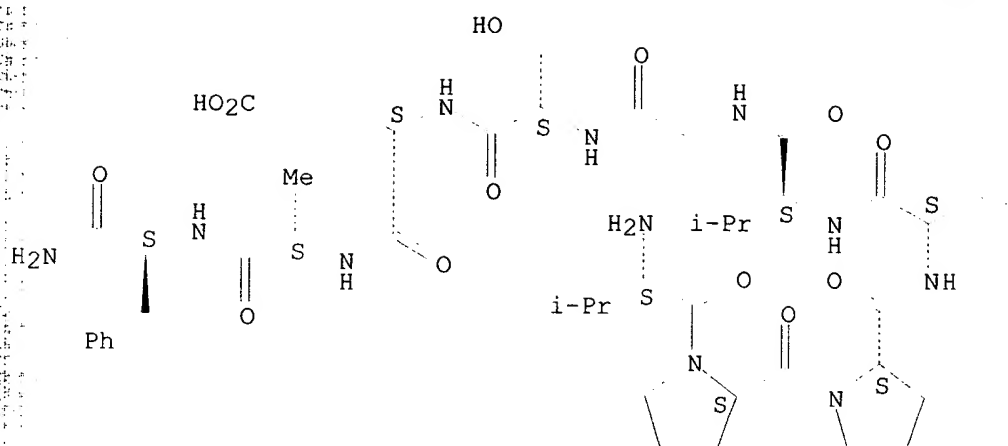
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RN 220198-84-5 CAPLUS
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Absolute stereochemistry.

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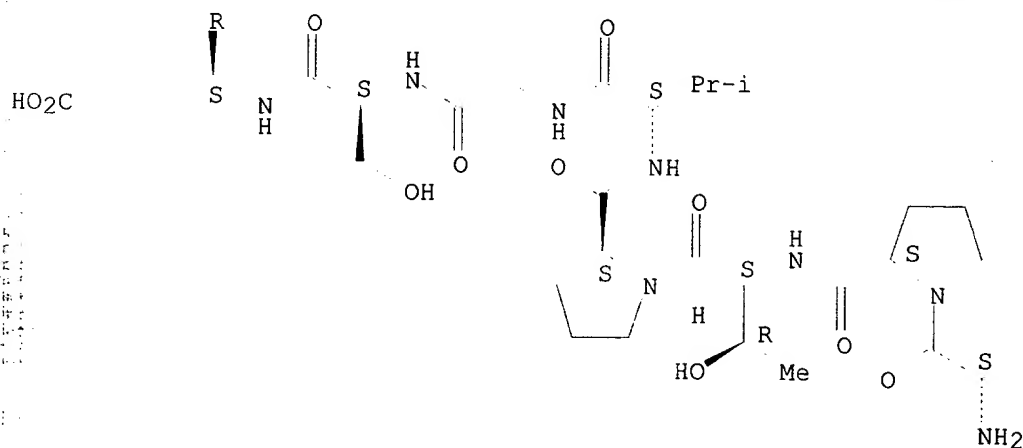
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NH₂

RN 220198-86-7 CAPLUS
 CN L-Phenylalaninamide, L-valyl-L-prolyl-L-threonyl-L-prolyl-L-valylglycyl-L-seryl-L- α -glutamyl-L-alanyl- (9CI) (CA INDEX NAME)

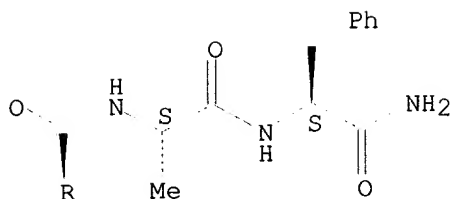
Absolute stereochemistry.

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Pr-i

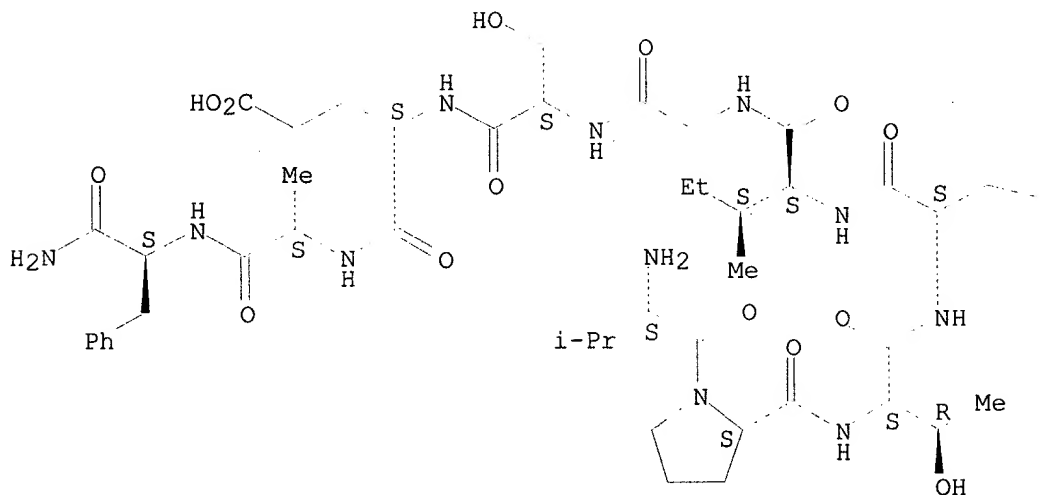
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L-Phenylalaninamide, L-valyl-L-prolyl-L-threonyl-L-asparaginyll-L-
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 NAME)

Absolute stereochemistry.

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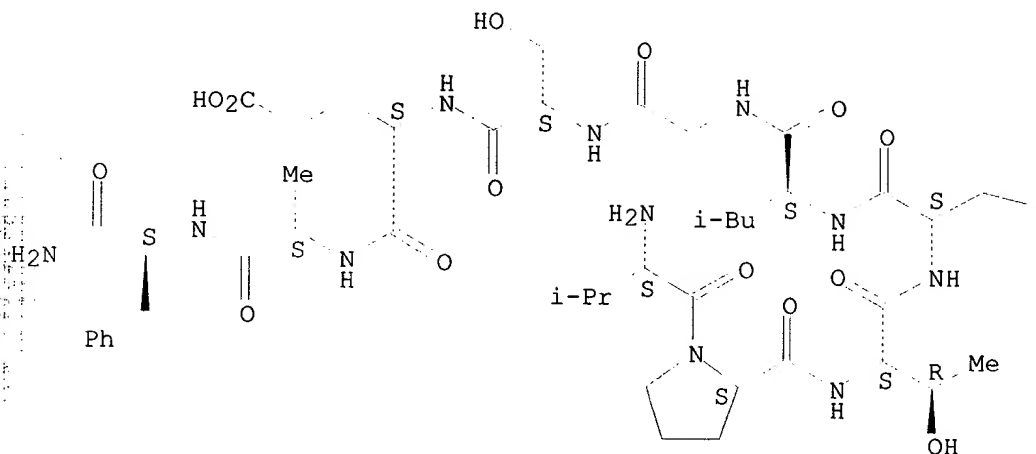
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NH₂

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Absolute stereochemistry.

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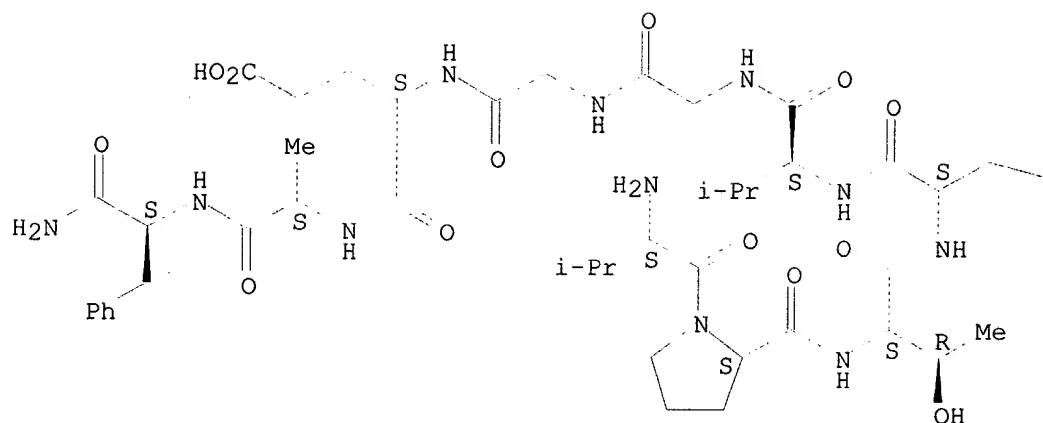
PAGE 1-B

NH₂

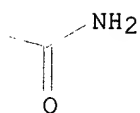
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Absolute stereochemistry.

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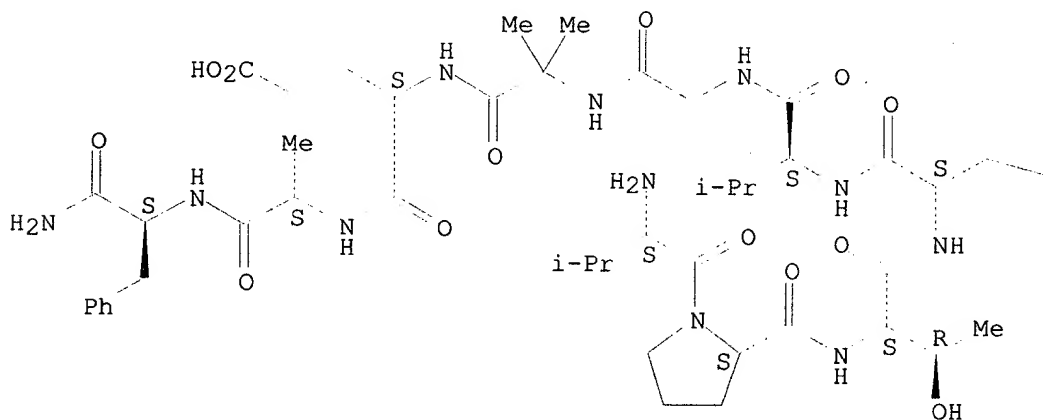


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Absolute stereochemistry.

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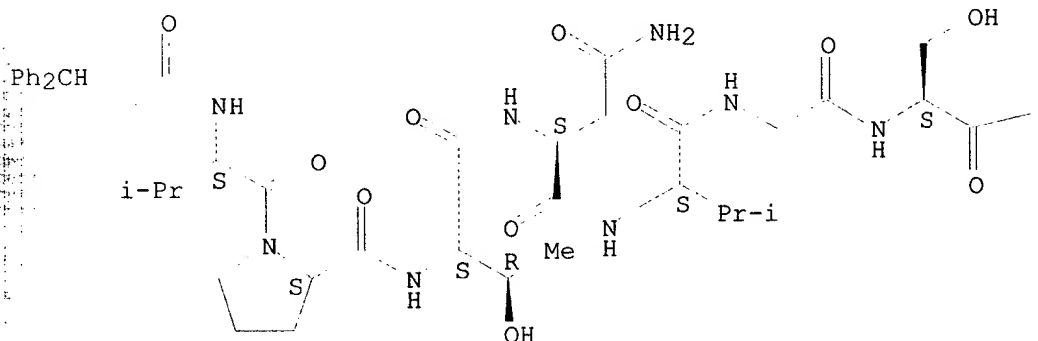
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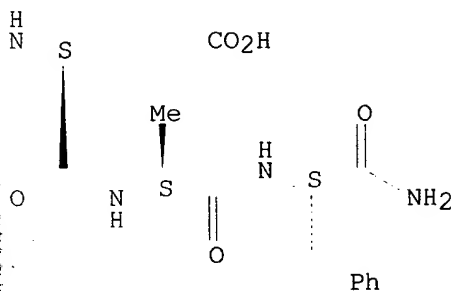
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Absolute stereochemistry.

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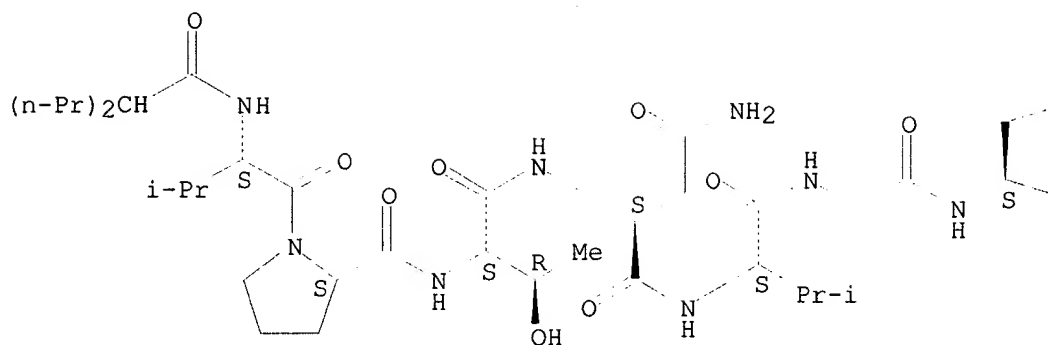
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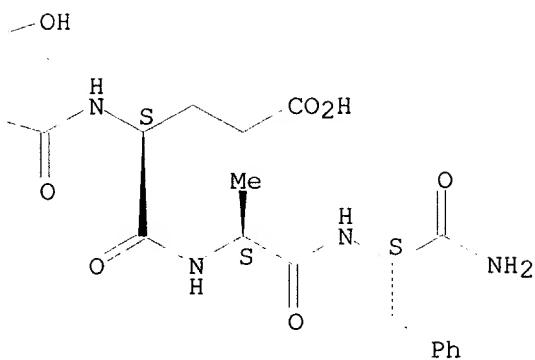
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Absolute stereochemistry.

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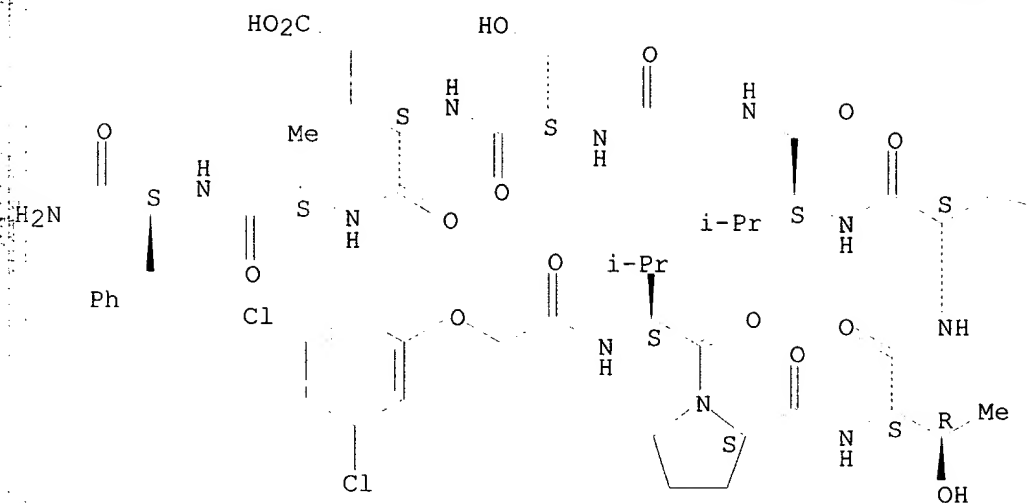


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Absolute stereochemistry.

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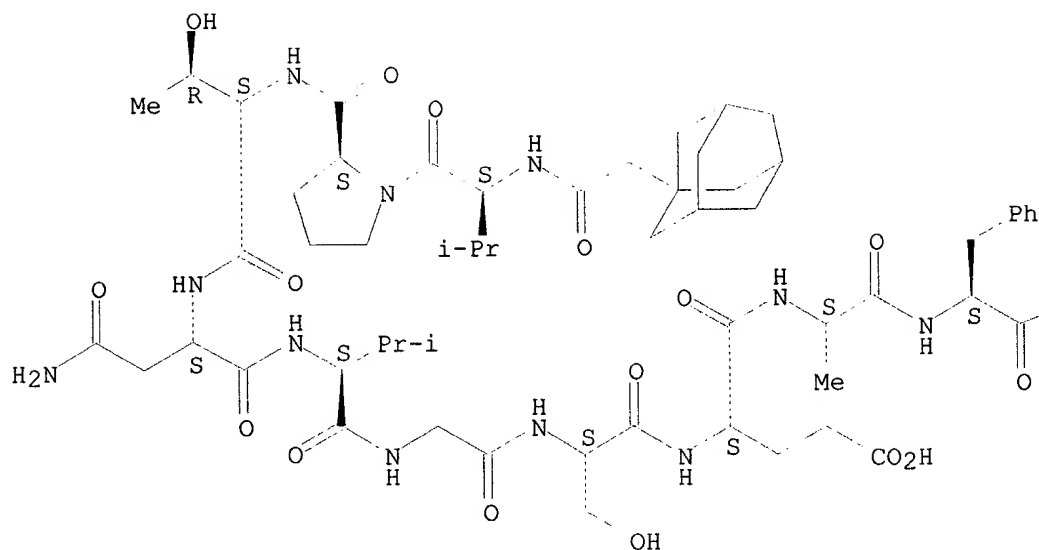
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NH₂

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Absolute stereochemistry.

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PAGE 1-B

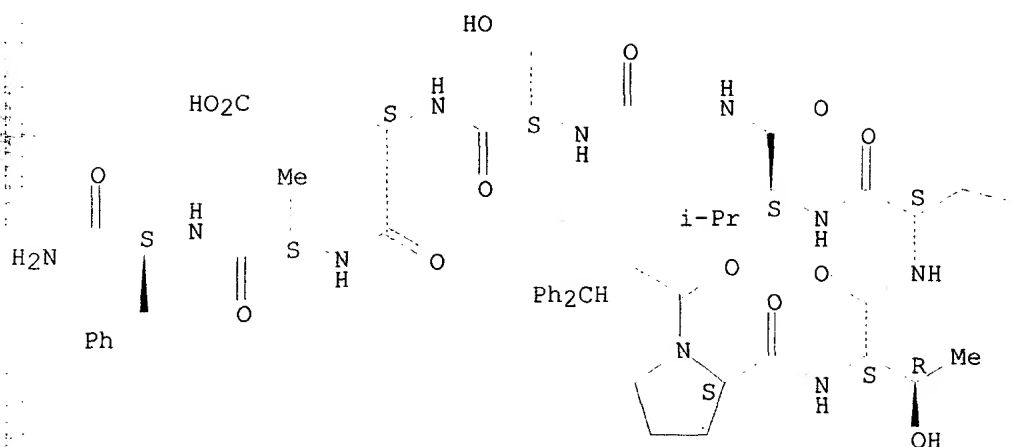
NH₂

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Absolute stereochemistry.

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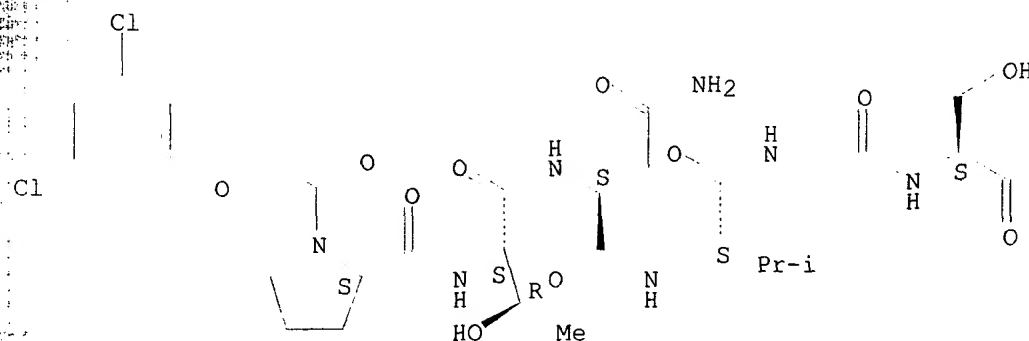
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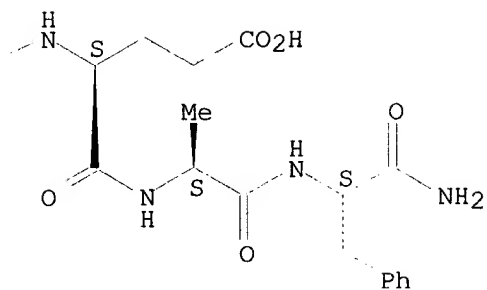
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Absolute stereochemistry.

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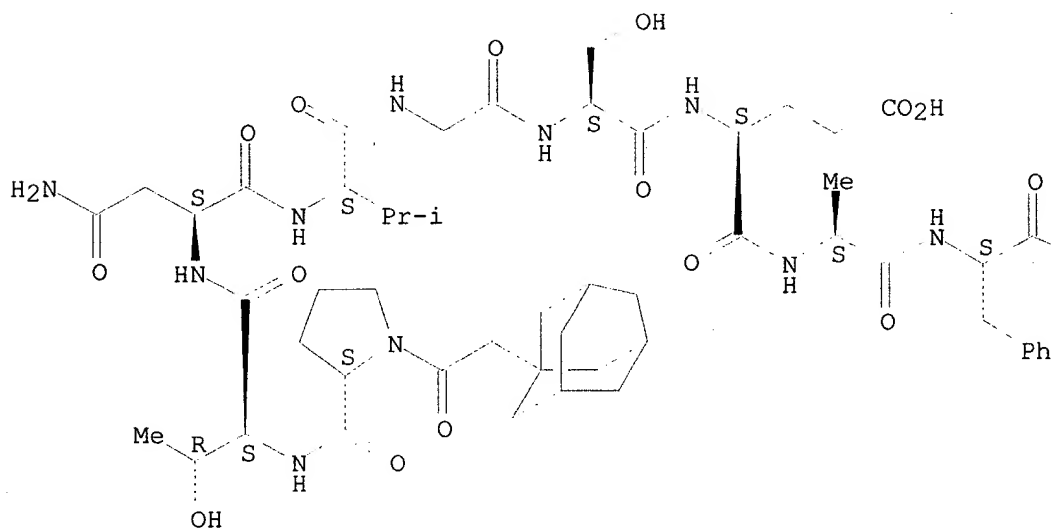


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Absolute stereochemistry.

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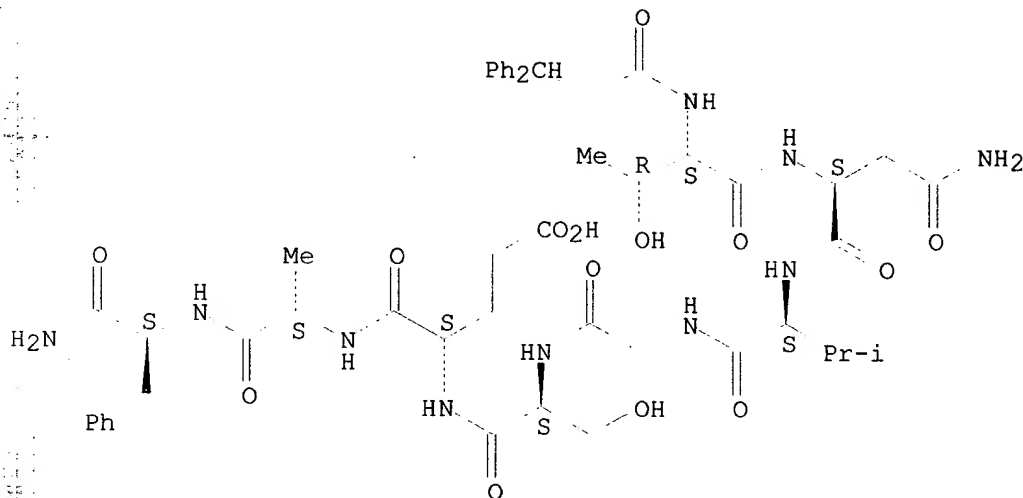


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NH2

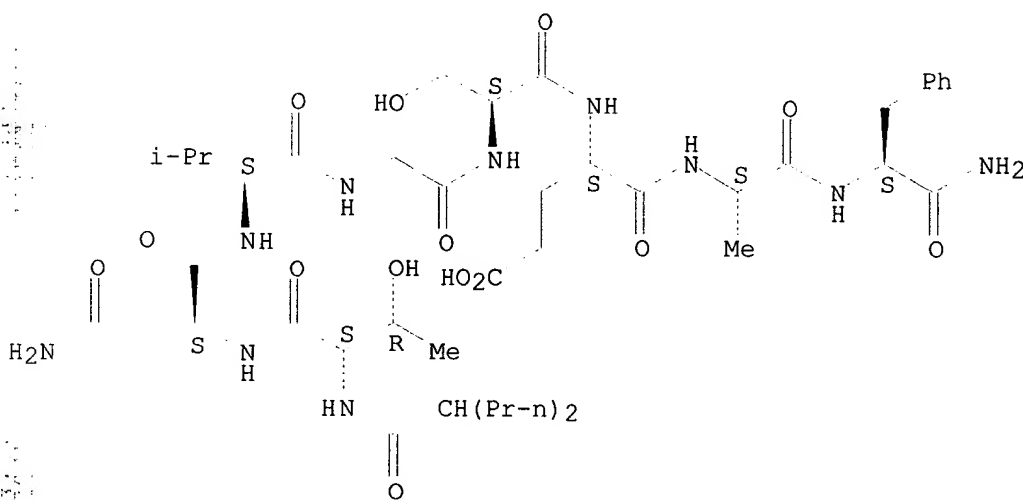
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Absolute stereochemistry.



RN 220199-01-9 CAPLUS
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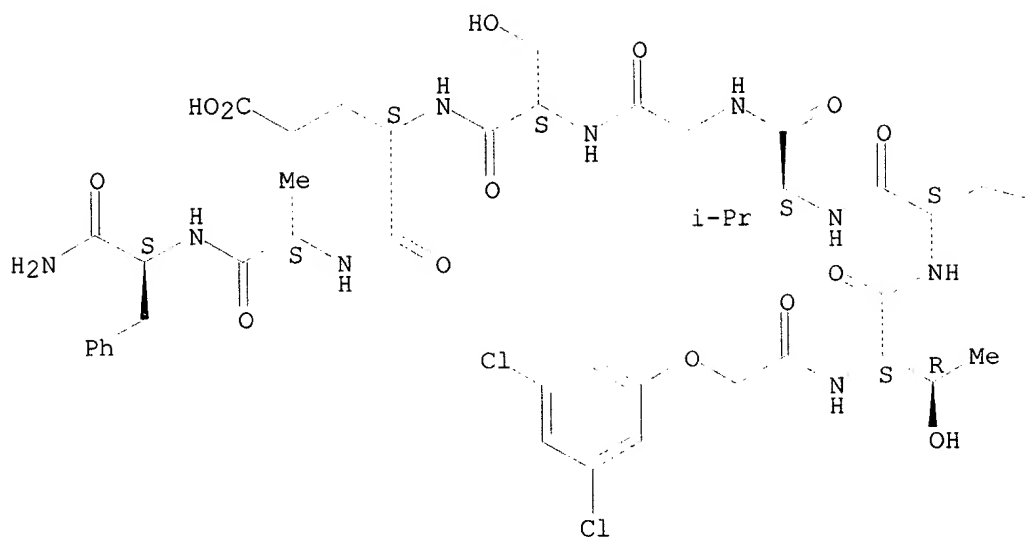
Absolute stereochemistry.



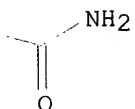
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Absolute stereochemistry.

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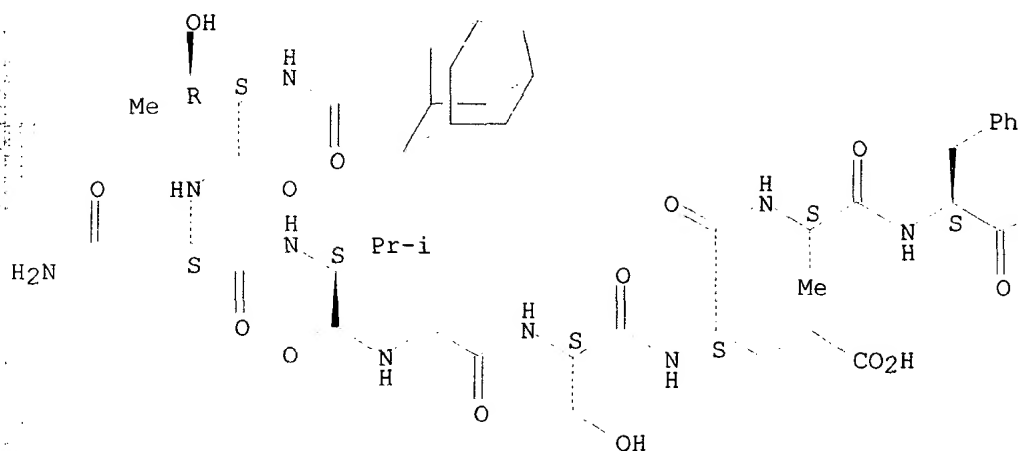
PAGE 1-B



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Absolute stereochemistry.

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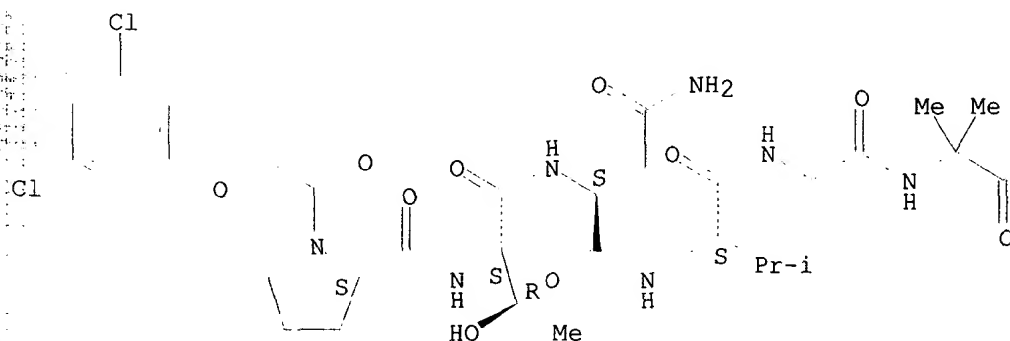
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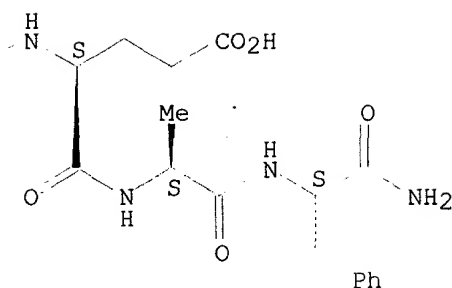
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Absolute stereochemistry.

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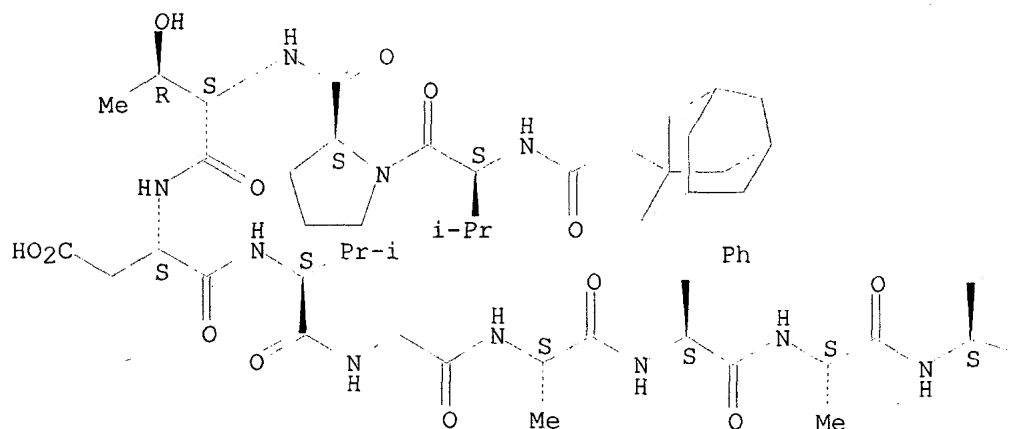


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Absolute stereochemistry.

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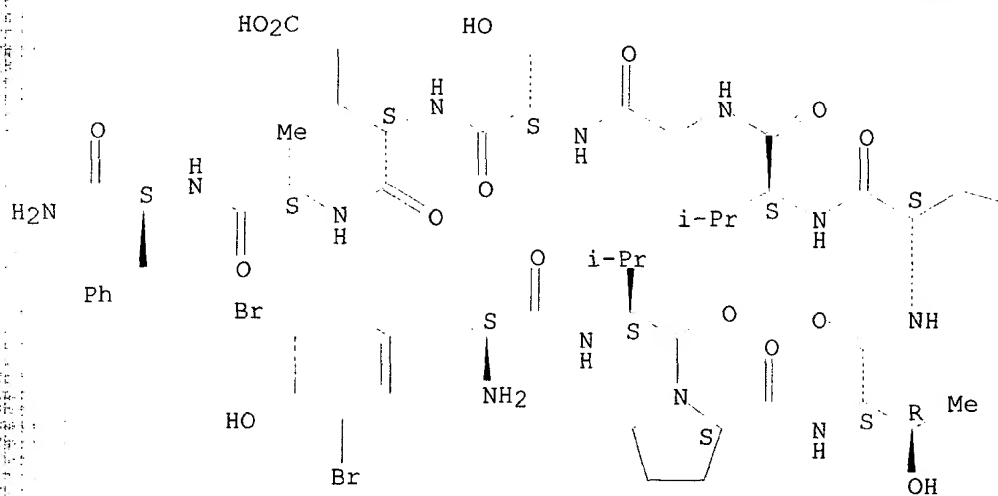
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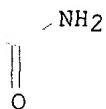
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Absolute stereochemistry.

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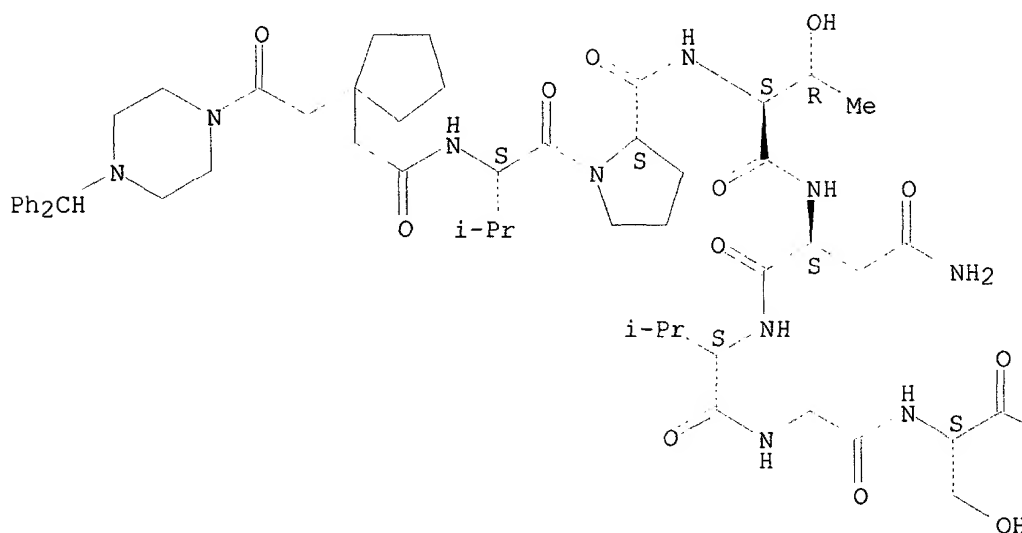
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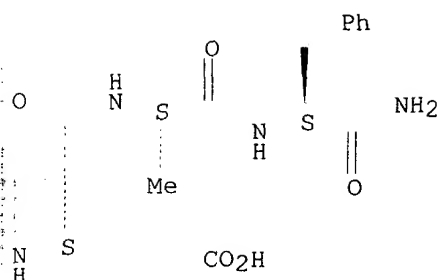
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Absolute stereochemistry.

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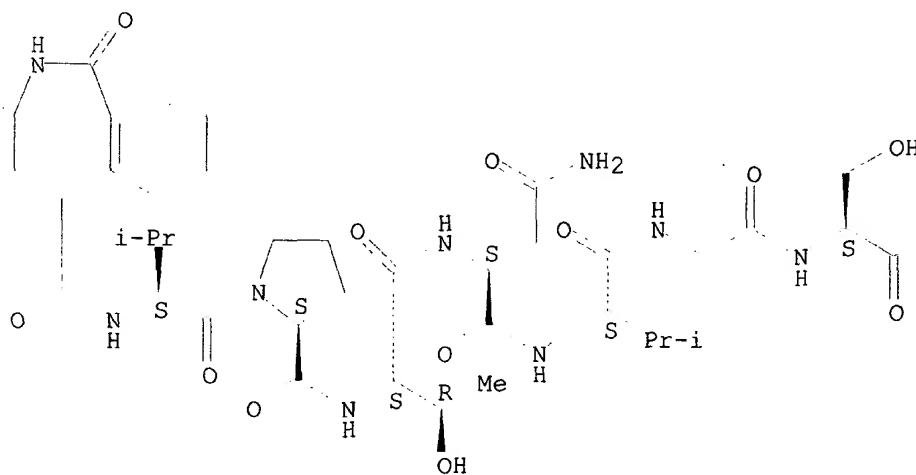


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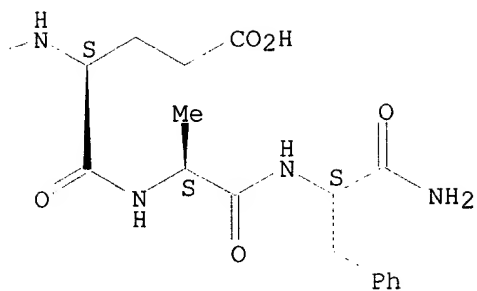
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Absolute stereochemistry.

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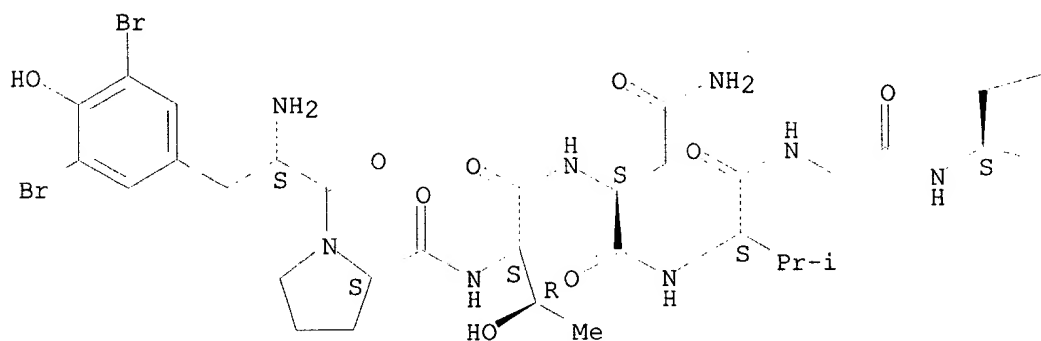
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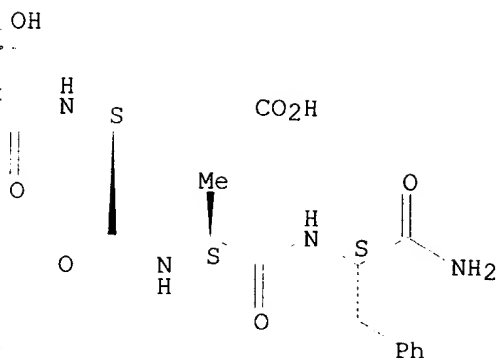
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Absolute stereochemistry.

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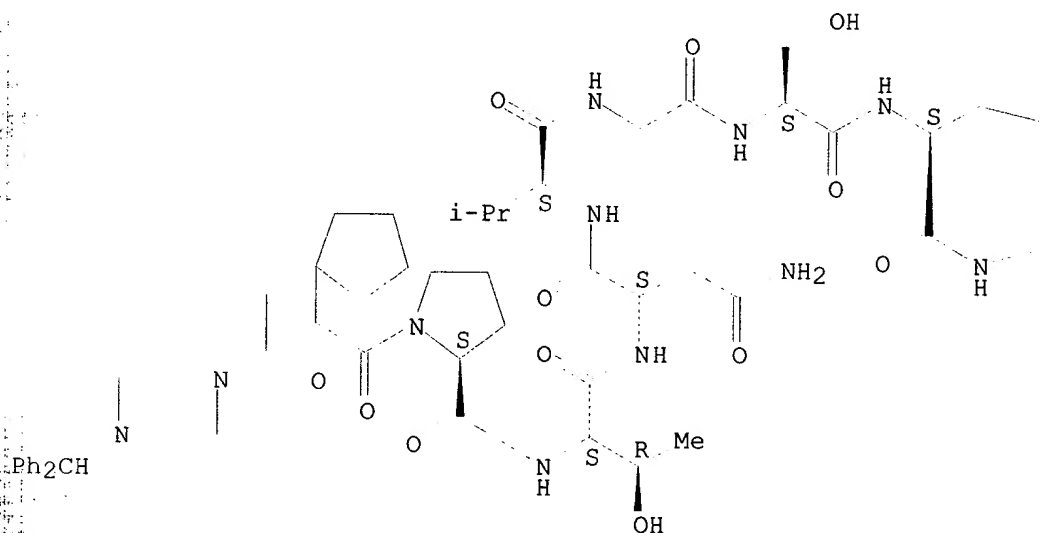


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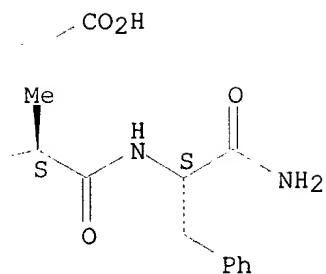
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Absolute stereochemistry.

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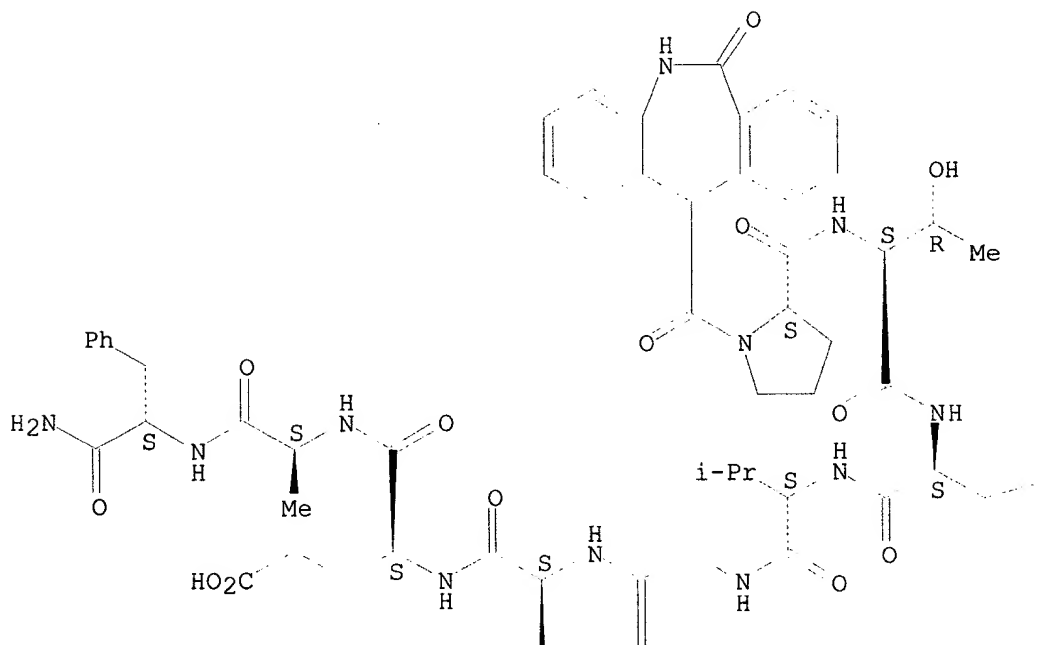


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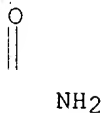
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Absolute stereochemistry.

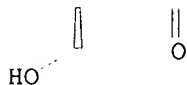
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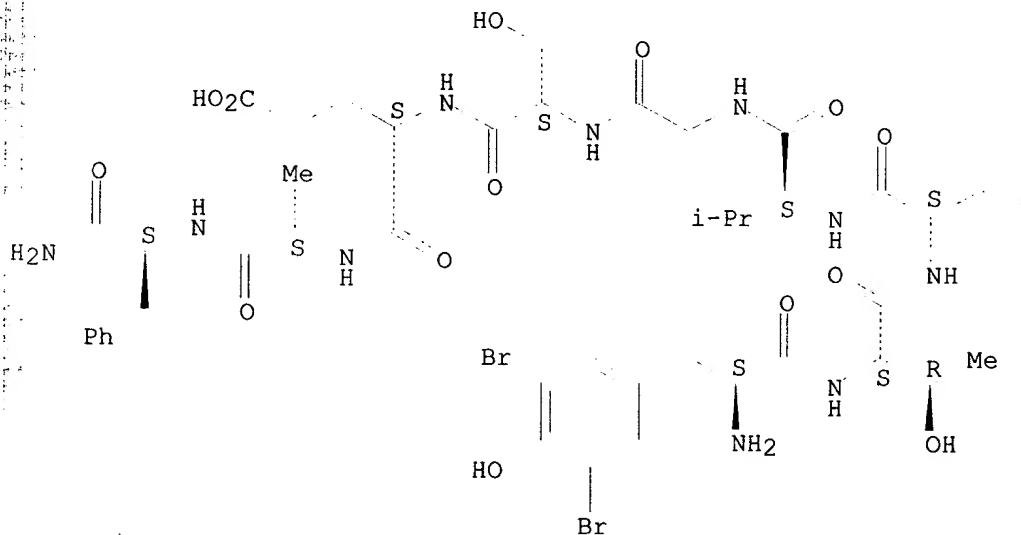
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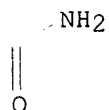
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Absolute stereochemistry.

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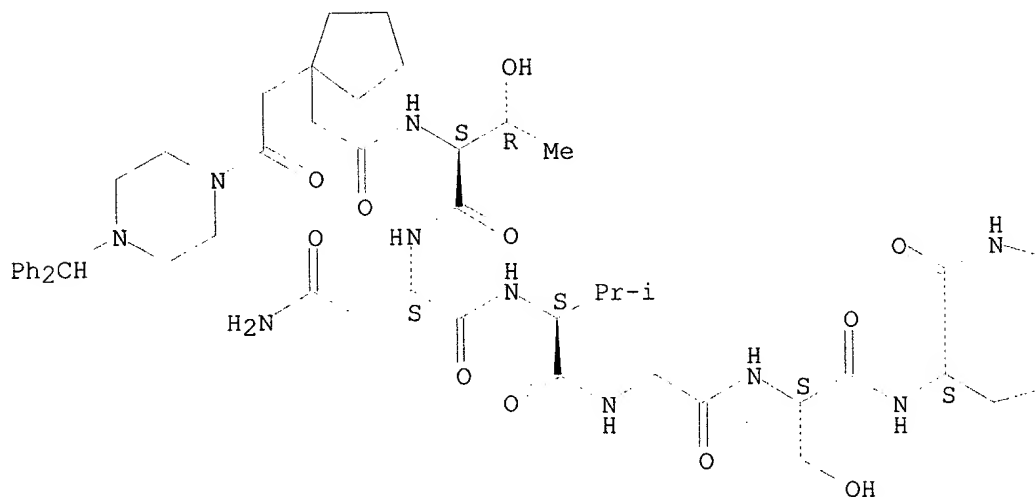
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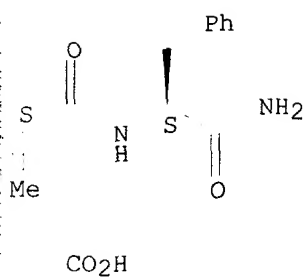
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Absolute stereochemistry.

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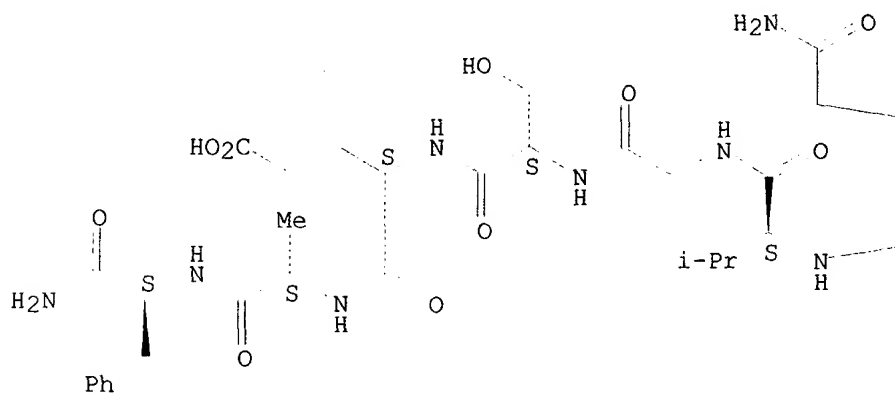
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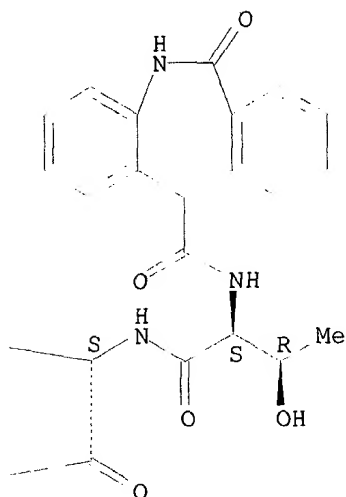
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Absolute stereochemistry.

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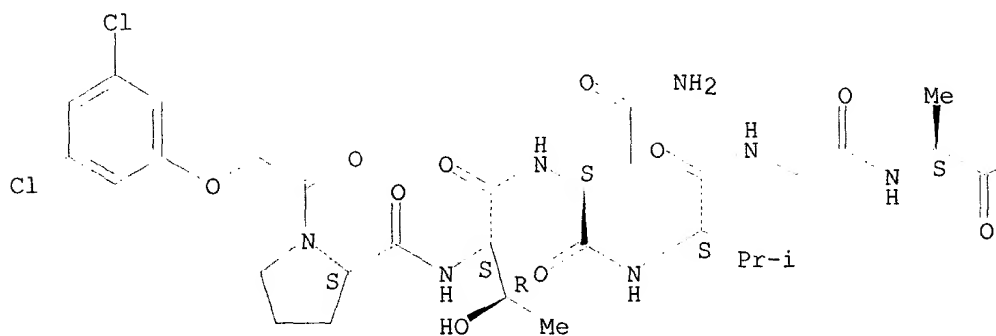


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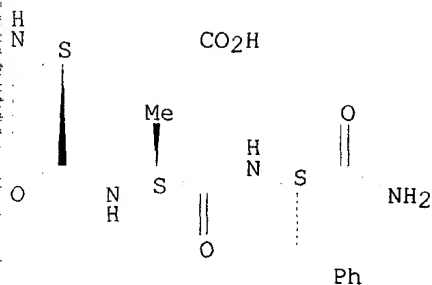
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Absolute stereochemistry.

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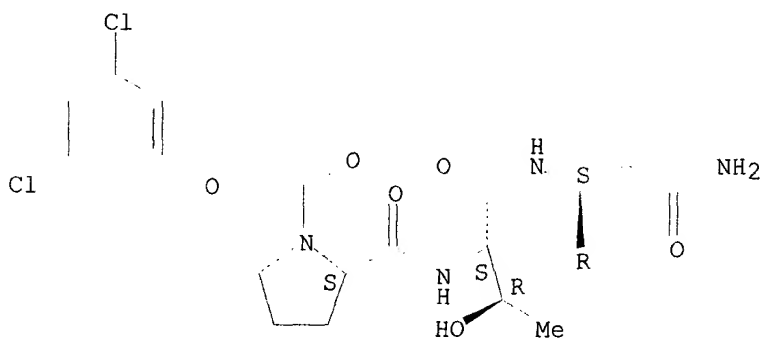


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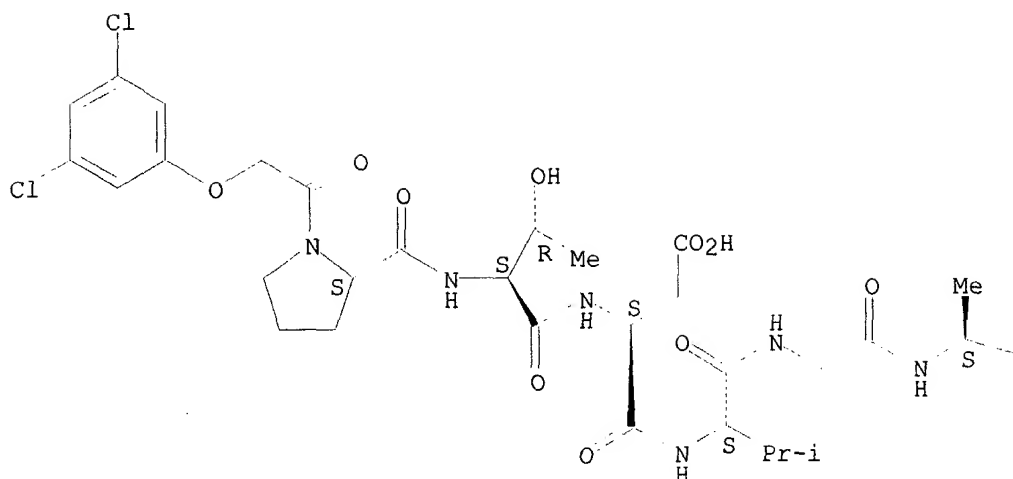
Absolute stereochemistry.



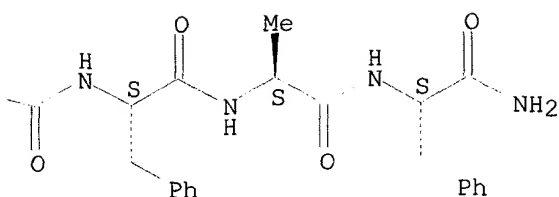
RN 220199-19-9 CAPLUS
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Absolute stereochemistry.

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L25 ANSWER 20 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:69021 CAPLUS

DOCUMENT NUMBER: 130:262591

TITLE: Reciprocal role of the AT1 receptor in modulating renal and neuronal AT1 mRNA expression

AUTHOR(S): Li, Jianping; Zhao, Huawei; Dipette, Donald J.; Supowit, Scott C.; Wang, Donna H.

CORPORATE SOURCE: Department of Internal Medicine, University of Texas Medical Branch, Galveston, TX, 77555-1065, USA

SOURCE: Journal of the American Society of Nephrology (1999), 10(1, Suppl. 11), S18-S22

CODEN: JASNEU; ISSN: 1046-6673

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB This study was designed to explore the mechanisms mediating the expression of the type 1 angiotensin II (AngII) receptor (AT1) in neuronal and renal

tissues. Four groups of rats were given 1% NaCl in water and subjected to the renal reduced mass protocol (RRM), RRM + ramipril (Ram, 10 mg/kg per d), RRM + candesartan (Can, 10 mg/kg per d), or sham surgery. After 12 d, mean arterial pressure (MAP) was significantly higher in RRM rats than in RRM + Ram, RRM + Can, and sham-operated rats. Northern blot anal. showed that renal AT1 receptor mRNA levels (AT1 mRNA/18 rRNA) were significantly decreased in RRM (1.08. \pm .0.05) and RRM + Ram (0.82. \pm .0.02) compared with sham-operated rats (1.38. \pm .0.06) and that candesartan treatment caused a further decrease in renal AT1 mRNA content (0.73. \pm .0.07) compared with RRM. In contrast, dorsal root ganglia AT1 receptor mRNA content was significantly decreased in RRM (0.52. \pm .0.06) compared with sham-operated rats (1.18. \pm .0.07), and this decrease was abolished by ramipril (1.40. \pm .0.13) and candesartan treatment (1.56. \pm .0.11). RIA showed that levels (ng/mg protein) of calcitonin gene-related peptide (CGRP) in the dorsal root ganglia were significantly increased in RRM (1.60. \pm .0.11) but not in RRM + Ram (1.14. \pm .0.20) and RRM + Can (1.18. \pm .0.09), compared with sham-operated rats (0.94. \pm .0.05). Thus, RRM-induced downregulation of neuronal AT1 mRNA expression is mediated by AngII activation of the AT1 receptor, whereas an AT1-independent mechanism is operant in mediating renal AT1 gene expression. Furthermore, the inverse relationship between neuronal AT1 expression and CGRP content indicates that activation of the neuronal AT1 receptor inhibits CGRP synthesis in the dorsal root ganglia. The functional implications of these findings are discussed.

IT 87333-19-5, Ramipril

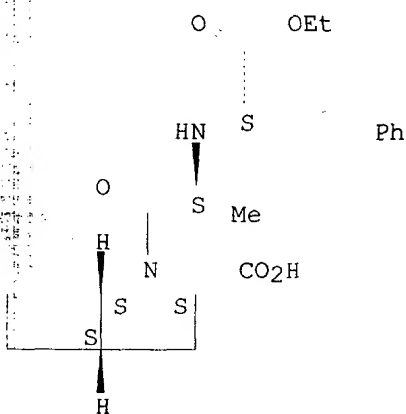
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antihypertensive effects of candesartan and ramipril are CGRP-independent)

RN 87333-19-5 CAPLUS

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

18

THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 21 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:44917 CAPLUS

DOCUMENT NUMBER: 130:100680

TITLE: Urologic irrigation solution and method for inhibition of pain, inflammation and spasm

INVENTOR(S): Demopoulos, Gregory A.; Pierce, Pamela A.; Herz, Jeffrey M.

Searched by Barb O'Bryen, STIC 308-4291

PATENT ASSIGNEE(S): Omeros Medical Systems, Inc., USA
SOURCE: U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 353,775,
abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5858017	A	19990112	US 1996-673171	19960626
CA 2206119	AA	19960627	CA 1995-2206119	19951212
CN 1175213	A	19980304	CN 1995-197538	19951212

PRIORITY APPLN. INFO.: US 1994-353775 B2 19941212

AB Disclosed are method and soln. for perioperatively inhibiting a variety of pain, inflammation and smooth muscle spasm processes resulting from urol. procedures. The soln. preferably includes multiple pain and inflammation inhibitory agents and spasm inhibitory agents at dil. concn. in a physiol. carrier, such as saline or lactated Ringer's soln. The soln. is introduced luminally to continuously irrigate a urol. structure during a urol. procedure for preemptive inhibition of pain and inflammation and smooth muscle spasm while avoiding undesirable side effects assocd. with oral, i.m., s.c. or i.v. application of larger doses of the agents. One preferred soln. to inhibit pain, inflammation, and spasm includes a serotonin₂ antagonist, a histamine₁ antagonist, a cyclooxygenase inhibitor, a neurokinin₂ antagonist, a purine_{2X} antagonist, an ATP-sensitive K⁺ channel antagonist, a Ca₂ channel antagonist, one or more nitric oxide donors, a bradykinin₁ antagonist and a bradykinin₂ antagonist.

IT 128270-60-0, Hirulog 129623-01-4 138614-30-9,
HOE 140

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

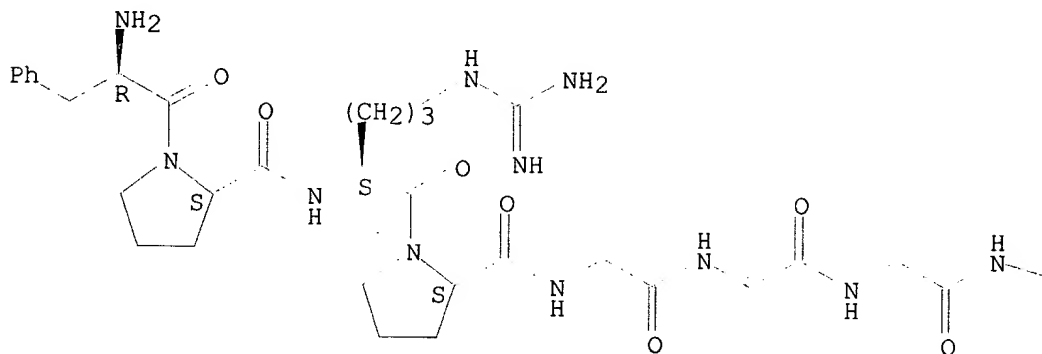
(urol. irrigation soln. contg. multiple receptor antagonists and agonists and enzyme inhibitors and activators for inhibition of pain and inflammation and spasm)

RN 128270-60-0 CAPLUS

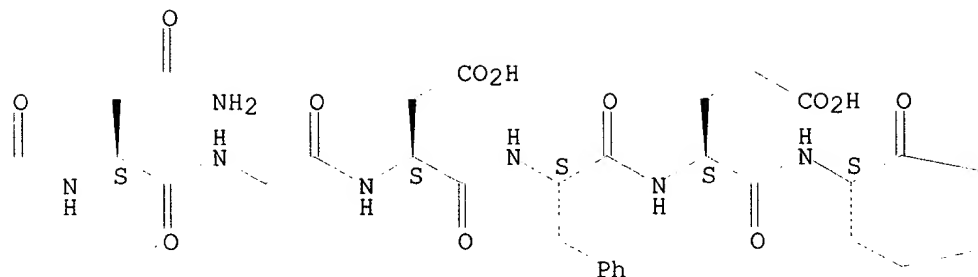
CN L-Leucine, D-phenylalanyl-L-prolyl-L-arginyl-L-prolylglycylglycylglycylglycyl-L-asparaginylglycyl-L-.alpha.-aspartyl-L-phenylalanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-isoleucyl-L-prolyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

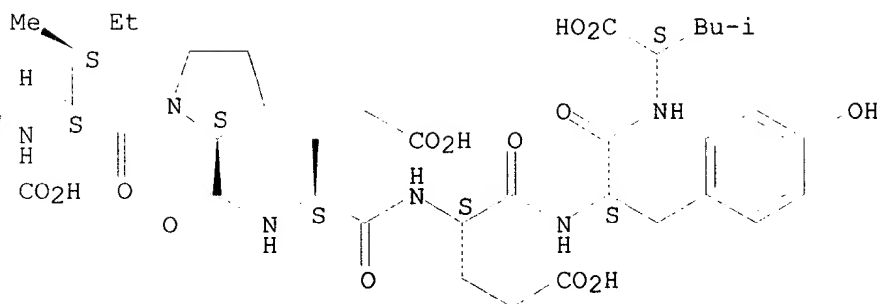
PAGE 1-A



PAGE 1-B



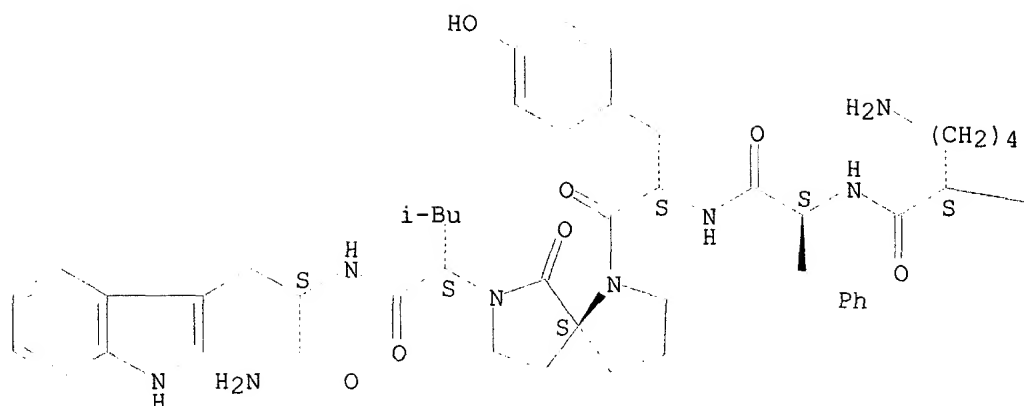
PAGE 1-C



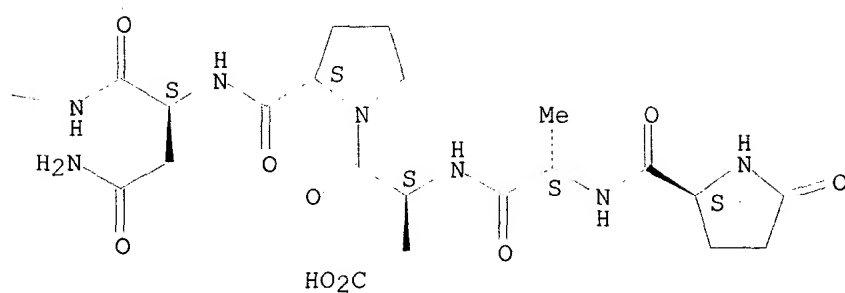
RN 129623-01-4 CAPLUS
 CN L-Tryptophanamide, 5-oxo-L-prolyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyl-L-lysyl-L-phenylalanyl-L-tyrosyl-(.alpha.S,5S)-.alpha.-(2-methylpropyl)-6-oxo-1,7-diazaspiro[4.4]nonane-7-acetyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



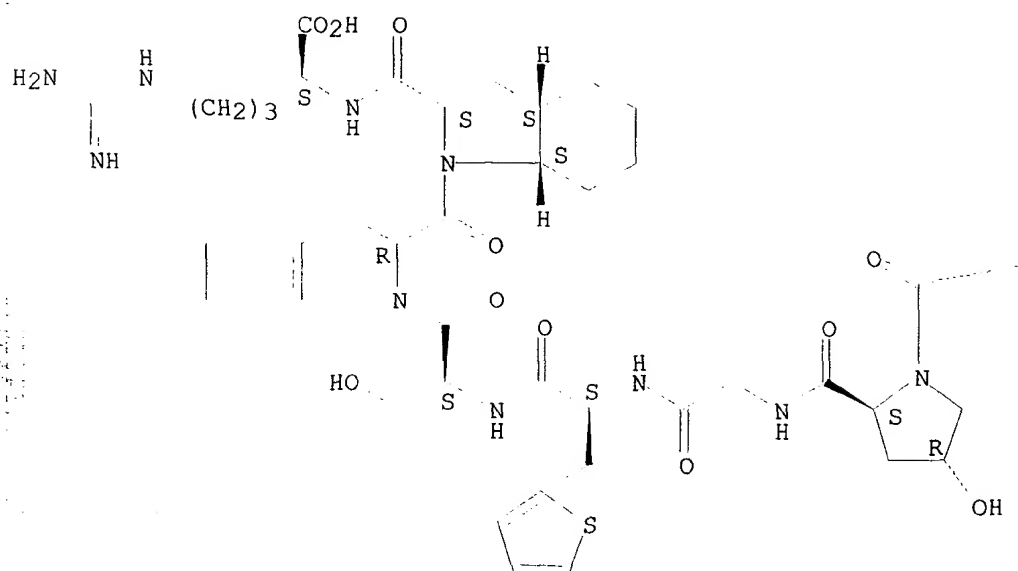
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CM 1

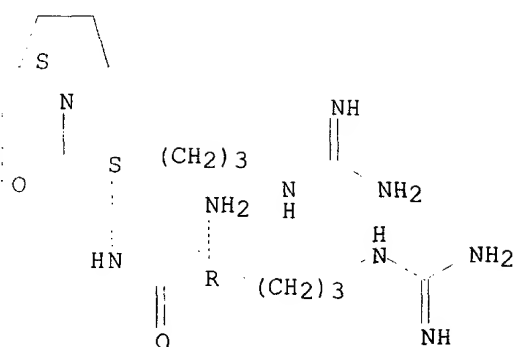
CRN 130308-48-4
 CMF C59 H89 N19 O13 S
 CDES *

Absolute stereochemistry.

PAGE 1-A

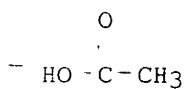


PAGE 1-B



CM 2

CRN 64-19-7
CMF C2 H4 O2



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 22 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:323132 CAPLUS
DOCUMENT NUMBER: 129:23447
TITLE: A method for treating tension-type headache
INVENTOR(S): Olesen, Jes; Bendtsen, Lars; Jensen, Rigmor; Madsen, Ulf
PATENT ASSIGNEE(S): Olesen, Jes, Den.; Bendtsen, Lars; Jensen, Rigmor; Madsen, Ulf
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9819674	A2	19980514	WO 1997-DK502	19971104
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9748632	A1	19980529	AU 1997-48632	19971104
AU 734490	B2	20010614		
EP 1011656	A2	20000628	EP 1997-911150	19971104
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
EP 1132082	A1	20010912	EP 2000-204625	19971104
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
US 6284794	B1	20010904	US 1999-304115	19990504
US 2002072543	A1	20020613	US 2001-941855	20010830
PRIORITY APPLN. INFO.:			DK 1996-1243	A 19961105
			US 1996-30294P	P 19961105
			EP 1997-911150	A3 19971104
			WO 1997-DK502	W 19971104
			US 1998-85413P	P 19980514
			US 1999-304115	A3 19990504

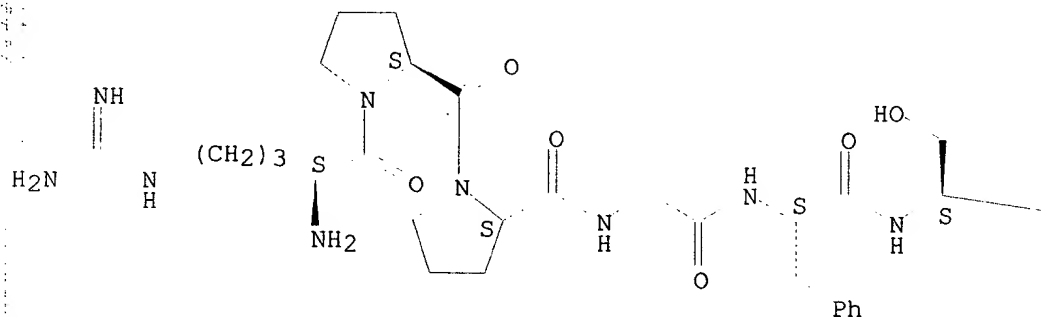
AB Tension-type headache is treated by interacting with neuronal transmission in relation to pain in connection with headache in a way which prevents or decreases sensitization of second order nociceptive neurons. In particular, treatment is performed by administration of an effective amt. of a substance which prevents or decreases central sensitization. Important examples of such substances are substances which interact with glutamate neurotransmission, such as glutamate receptor antagonists. Other examples are e.g. substances which interact with nitric oxide, such as nitric oxide synthase (NOS) inhibitors. According to a broader aspect of the invention, tension-type headache is treated by administration of substances which are effective in preventing or decreasing pain in connection with tension-type headache. An addnl. aspect of the invention relates to treatment of tension-type headache by administration of substances which substantially inhibit the activity of NOS. Evidence for central sensitization in chronic myofascial pain, as well as mechanisms of spontaneous tension-type headaches, are also described. Gabapentin and dextromethorphen had a prophylactic effect on chronic tension-type

headaches.

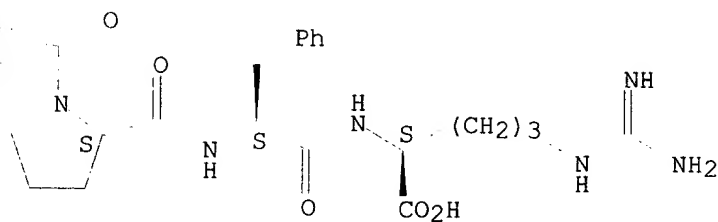
IT 58-82-2, Bradykinin 33507-63-0, Substance P
RL: BAC (Biological activity or effector, except adverse); BPR
(Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(prodn. and release and action; tension-type headache treatment)
RN 58-82-2 CAPLUS
CN Bradykinin (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



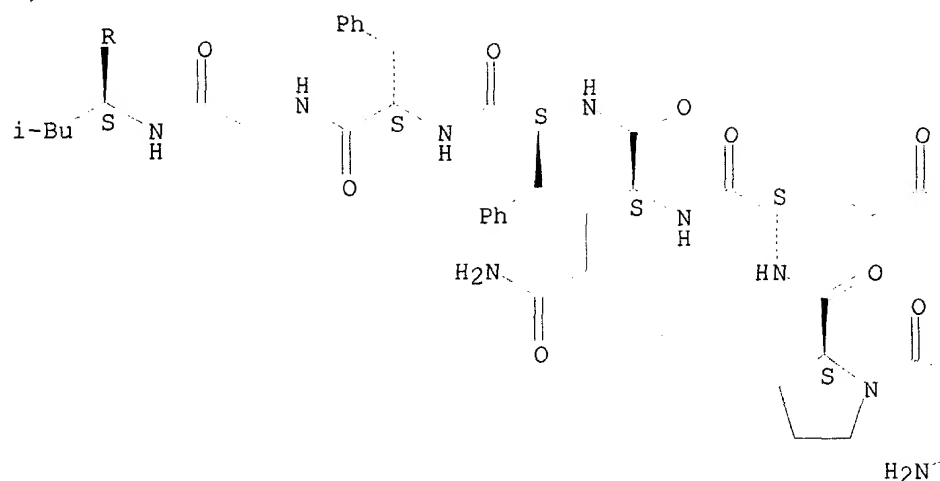
PAGE 1-B



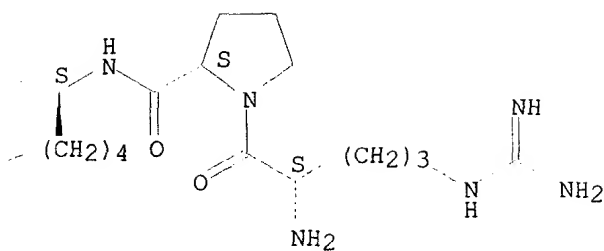
RN 33507-63-0 CAPLUS
CN Substance P (9CI) (CA INDEX NAME)

Absolute stereochemistry.

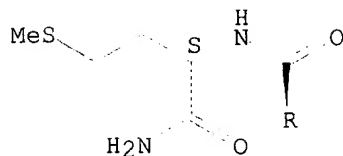
PAGE 1-A



PAGE 1-B

NH₂

PAGE 2-A



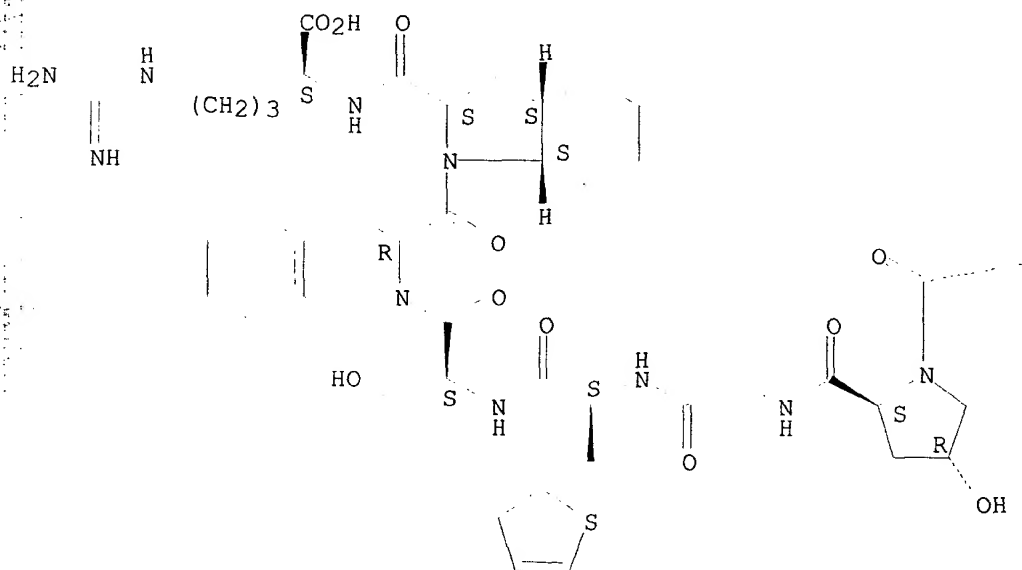
IT 130308-48-4, Icatibant 130308-48-4D, Icatibant, derivs.
 138449-07-7, FK 888 138449-07-7D, FK 888, derivs.
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)

(tension-type headache treatment)

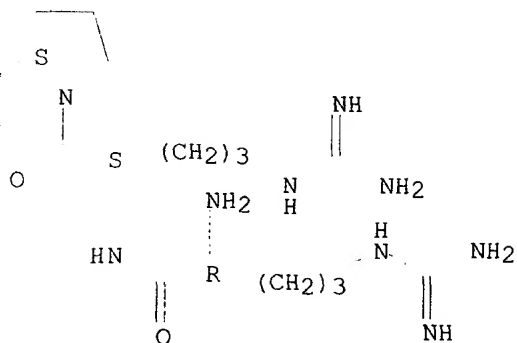
RN 130308-48-4 CAPLUS
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 (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



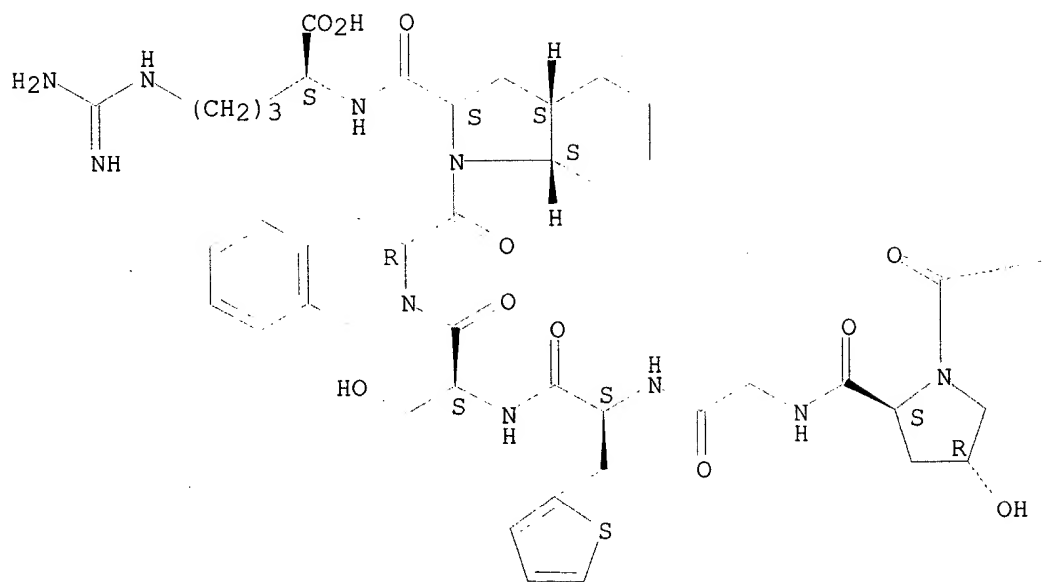
PAGE 1-B



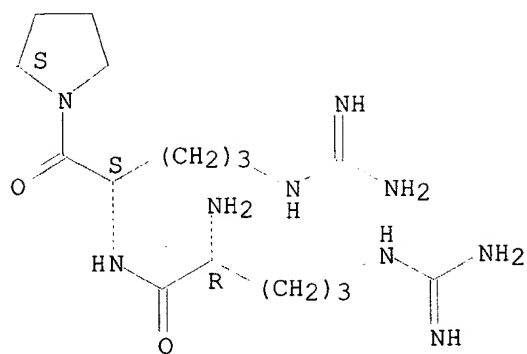
RN 130308-48-4 CAPLUS
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Absolute stereochemistry.

PAGE 1-A

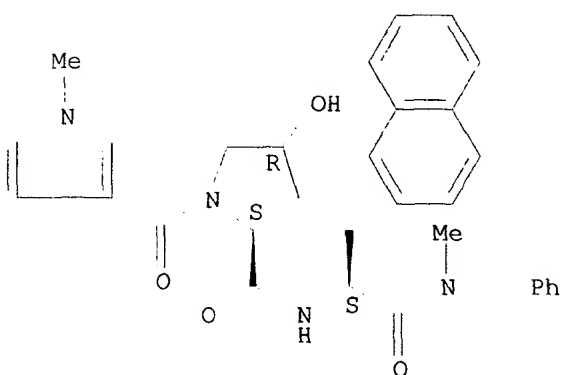


PAGE 1-B



RN 138449-07-7 CAPLUS
CN L-Alaninamide, (4R)-4-hydroxy-1-[(1-methyl-1H-indol-3-yl)carbonyl]-L-prolyl-N-methyl-3-(2-naphthalenyl)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

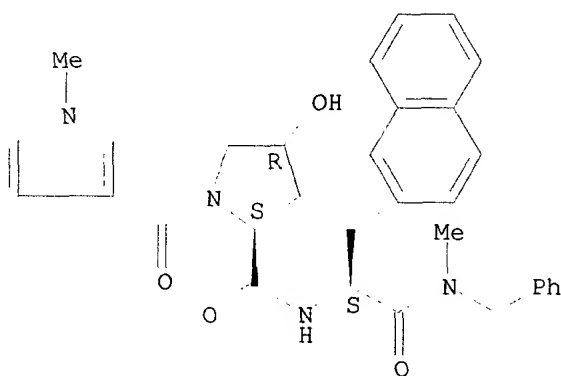
Absolute stereochemistry.



RN 138449-07-7 CAPLUS

CN L-Alaninamide, (4R)-4-hydroxy-1-[(1-methyl-1H-indol-3-yl)carbonyl]-L-prolyl-N-methyl-3-(2-naphthalenyl)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 23 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:197358 CAPLUS

DOCUMENT NUMBER: 128:257695

TITLE: Preparation of modified amino acids and their use as calcitonin gene-related peptide antagonists in pharmaceutical compositions

INVENTOR(S): Rudolf, Klaus; Eberlein, Wolfgang; Engel, Wolfhard; Pieper, Helmut; Doods, Henri; Hallermayer, Gerhard; Entzeroth, Michael; Wienen, Wolfgang

PATENT ASSIGNEE(S): Karl Thomae G.m.b.H., Germany; Rudolf, Klaus; Eberlein, Wolfgang; Engel, Wolfhard; Pieper, Helmut; Doods, Henri; Hallermayer, Gerhard; Entzeroth, Michael; Wienen, Wolfgang

SOURCE: PCT Int. Appl., 461 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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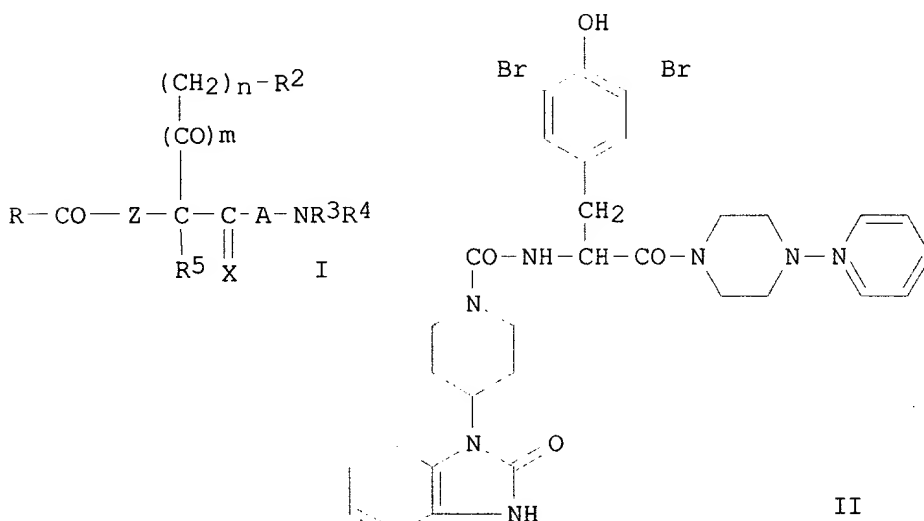
WO 9811128 A1 19980319 WO 1997-EP4862 19970908
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,
KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG
DE 19636623 A1 19980312 DE 1996-19636623 19960910
DE 19720011 A1 19981119 DE 1997-19720011 19970514
AU 9741196 A1 19980402 AU 1997-41196 19970908
AU 721035 B2 20000622
EP 927192 A1 19990707 EP 1997-938928 19970908
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IE, SI, LT, LV, FI, RO
BR 9712023 A 19990831 BR 1997-12023 19970908
JP 2000505100 T2 20000425 JP 1998-513227 19970908
NO 9901130 A 19990505 NO 1999-1130 19990309
KR 2000044040 A 20000715 KR 1999-702008 19990310
US 6344449 B1 20020205 US 1999-254281 19991012
US 2001036946 A1 20011101 US 2001-789391 20010221

PRIORITY APPLN. INFO.:

DE 1996-19636623 A 19960910
DE 1997-19720011 A 19970514
WO 1997-EP4862 W 19970908
US 1999-254281 A1 19991012

OTHER SOURCE(S):
GI

MARPAT 128:257695



AB The invention concerns modified amino acids of general formula I [A = bond, CX; Z = CH₂, NR₁; R₁ = H, alkyl, phenyl-alkyl; X = O, H, H; n = 1-2; m = 0-1; R = (substituted)alkyl; R₂ = Ph, (substituted) (hetero) (bi) cycle; R₃ = H, (substituted)alkyl, Ph, pyridinyl; R₄ = H, (substituted)alkyl; R₃R₄ = (hetero)cycle; R₅ = H, alkyl, alkoxy-carbonyl, PhCH₂], pharmaceuticals contg. these compds., their use and the method for their prodn., as well as their use for the prodn. and purifn. of antibodies and as marked compds. in RIA and ELISA assays and as diagnostic or analytic auxiliary agents in neurotransmitter research. Thus, 3,5-dibromo-N²-[4-(1,3-dihydro-2(2H)-oxo-benzimidazol-1-yl)-1-piperidinyl]carbonyl-D-tyrosine was reacted with 1-(4-pyridinyl)-piperazine, to give II(22%).

Title compds. show human calcitonin gene related peptide (CGRP) antagonist activity; in in-vitro binding studies with Sk-N-MC-cells, I had IC50 .ltoreq.10000 nM, and in the same system, had CGRP-antagonist activity at doses from 10-11 to 10-6 M.

L25 ANSWER 24 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:186625 CAPLUS

DOCUMENT NUMBER: 128:230701

TITLE: Preparation of varied amino acids as

calcitonin gene-related

peptide antagonists in

pharmaceutical compositions

INVENTOR(S):

Rudolf, Klaus; Eberlein, Wolfgang; Engel, Wolfhard;

Pieper, Helmut; Doods, Henri; Hallermayer, Gerhard;

Entzeroth, Michael; Wienen, Wolfgang

PATENT ASSIGNEE(S):

Karl Thomae G.m.b.H., Germany

SOURCE:

Ger. Offen., 142 pp.

CODEN: GWXXBX

DOCUMENT TYPE:

Patent

LANGUAGE:

German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19636623	A1	19980312	DE 1996-19636623	19960910
WO 9811128	A1	19980319	WO 1997-EP4862	19970908
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AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:				
GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9741196	A1	19980402	AU 1997-41196	19970908
AU 721035	B2	20000622		
EP 927192	A1	19990707	EP 1997-938928	19970908
R:				
AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9712023	A	19990831	BR 1997-12023	19970908
CN 1230196	A	19990929	CN 1997-197772	19970908
JP 2000505100	T2	20000425	JP 1998-513227	19970908
ZA 9708083	A	19991217	ZA 1997-8083	19970909
NO 9901130	A	19990505	NO 1999-1130	19990309
US 6344449	B1	20020205	US 1999-254281	19991012

PRIORITY APPLN. INFO.:

DE 1996-19636623 A 19960910

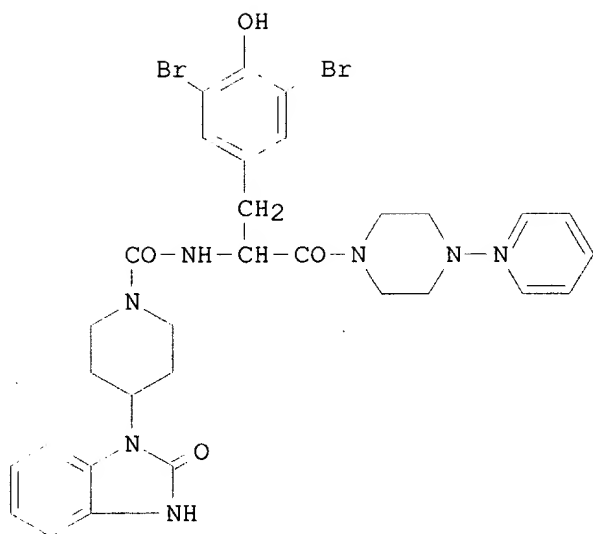
DE 1997-19720011 A 19970514

WO 1997-EP4862 W 19970908

OTHER SOURCE(S):

MARPAT 128:230701

GI



II

AB Title compds. RCOZCR1R2C(:X)ANR3R4 [(I); R = (substituted) alkyl; R1 = H, alkyl, PhCH2; R2 = (CO)m(CH2)nR5; m = 0, 1; n = 1, 2; R5 = Ph, heterocycle; X = O, (H,H); Z = CH2, NR6; R6 = H, alkyl, phenyl-alkyl; A = bond, proline; R3 = H, substituted alkyl, Ph, pyridinyl; R4 = H, substituted alkyl; NR3R4 = (substituted) heterocycle], useful as calcitonin gene-related peptide (CGRP) antagonists, were prepd. Thus, 3,5-dibromo-N2-[4-(1,3-dihydro-2(2H)-oxo-benzimidazol-1-yl)-1-piperidinyl]carbonyl-D-tyrosine was reacted with 1-(4-pyridinyl)-piperazine, to give II (22%). In in-vitro binding studies with human CGRP-receptors, I had IC50 .ltoreq.10000 nM; in CGRP-antagonist in vitro tests, I was effective at doses from 10-11 to 10-5 M.

IT 204695-88-5P 204695-92-1P 204697-47-2P
204697-53-0P 204697-79-0P 204697-82-5P
204697-83-6P 204697-84-7P 204697-86-9P
204697-93-8P 204697-95-0P 204698-27-1P
204698-31-7P 204698-33-9P 204698-34-0P
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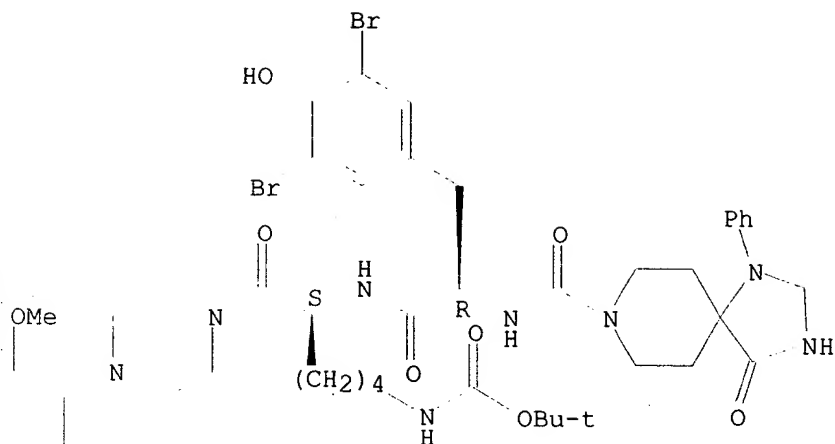
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of amino acids and their use as **calcitonin gene-related peptide antagonists** in pharmaceutical compns.)

RN 204695-88-5 CAPLUS

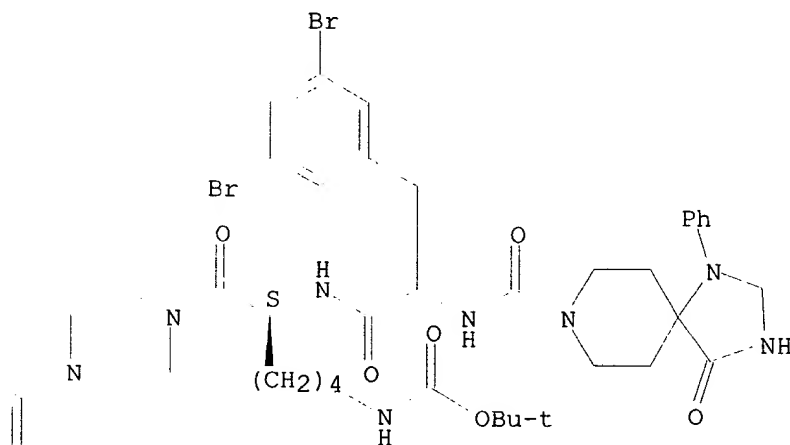
CN Carbamic acid, [5-[[3-(3,5-dibromo-4-hydroxyphenyl)-1-oxo-2-[[4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]dec-8-yl)carbonyl]amino]propyl]amino]-6-[4-(2-methoxyphenyl)-1-piperazinyl]-6-oxohexyl]-, 1,1-dimethylethyl ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



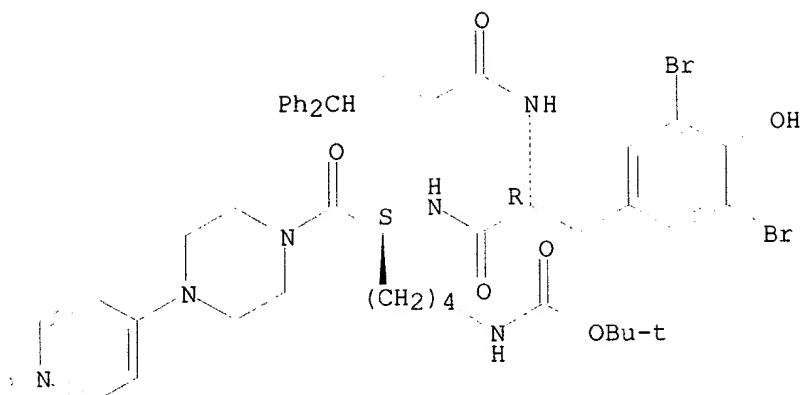
RN 204695-92-1 CAPLUS
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 (CA INDEX NAME)

Absolute stereochemistry.



RN 204697-47-2 CAPLUS
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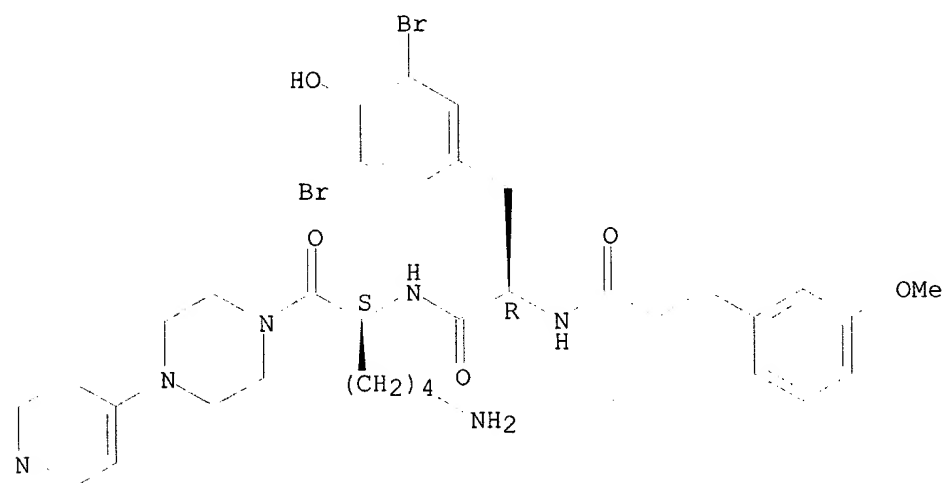
Absolute stereochemistry.



RN 204697-53-0 CAPLUS

CN Benzenepropanamide, N-[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]-3,5-dibromo-4-hydroxy-.alpha.-[[3-(3-methoxyphenyl)-1-oxopropyl]amino]-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

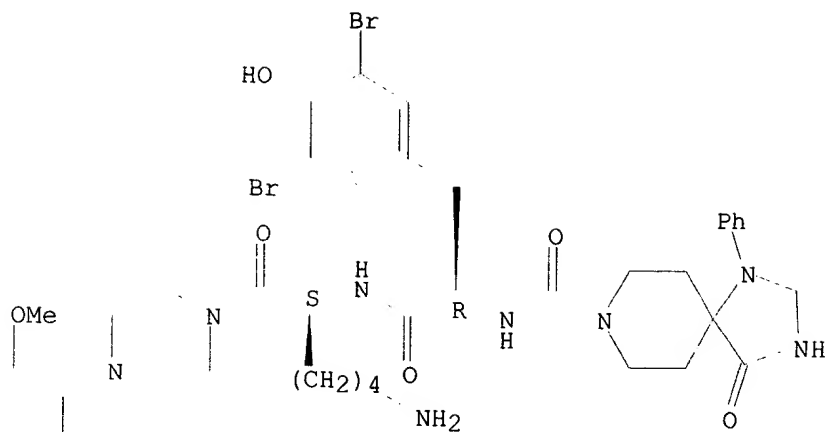
Absolute stereochemistry.



RN 204697-79-0 CAPLUS

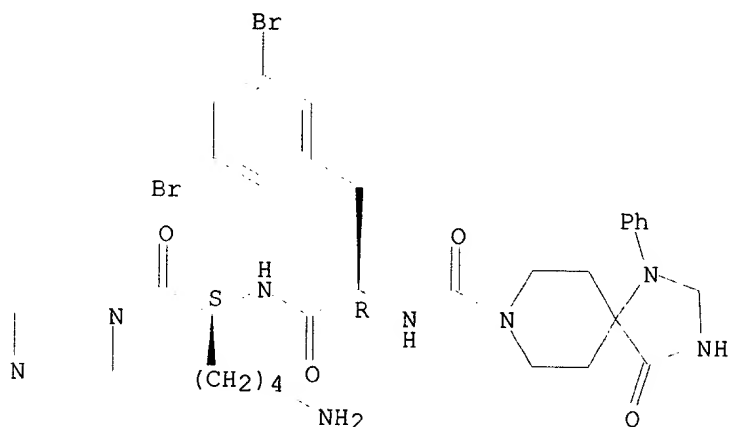
CN 1,3,8-Triazaspiro[4.5]decane-8-carboxamide, N-[2-[[5-amino-1-[[4-(2-methoxyphenyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-4-oxo-1-phenyl-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



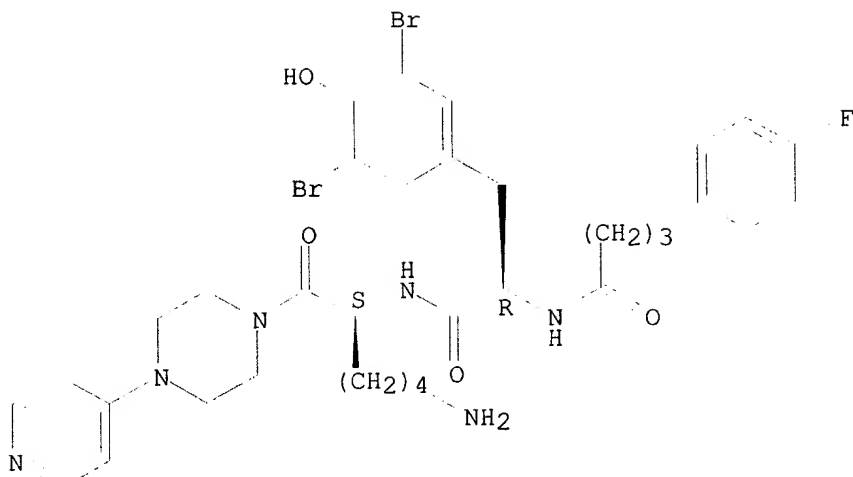
RN 204697-82-5 CAPLUS
 CN 1,3,8-Triazaspiro[4.5]decane-8-carboxamide, N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromophenyl)methyl]-2-oxoethyl]-4-oxo-1-phenyl-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204697-83-6 CAPLUS
 CN Benzenebutanamide, N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-4-fluoro-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

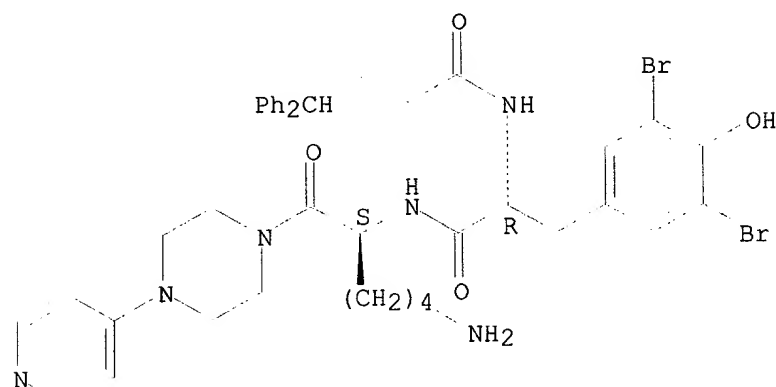
Absolute stereochemistry.



RN 204697-84-7 CAPLUS

CN Benzenebutanamide, N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-.gamma.-phenyl-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

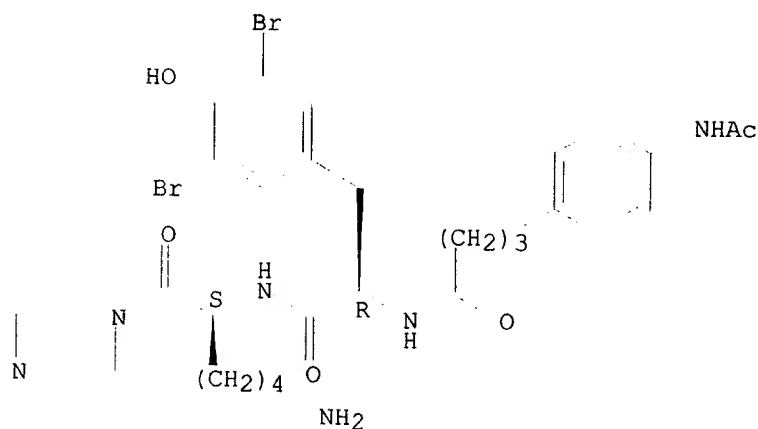
Absolute stereochemistry.



RN 204697-86-9 CAPLUS

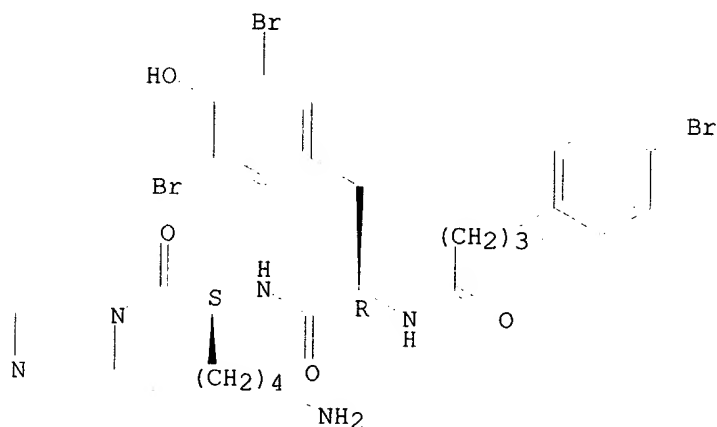
CN Benzenebutanamide, 4-(acetylamino)-N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



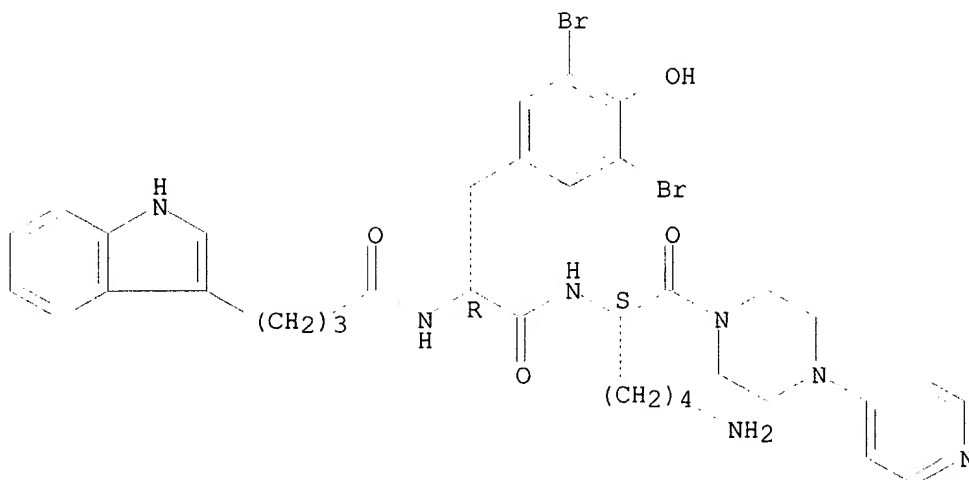
RN 204697-93-8 CAPLUS
 CN Benzenebutanamide, N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-4-bromo-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

— Absolute stereochemistry.



RN 204697-95-0 CAPLUS
 CN 1H-Indole-3-butanamide, N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

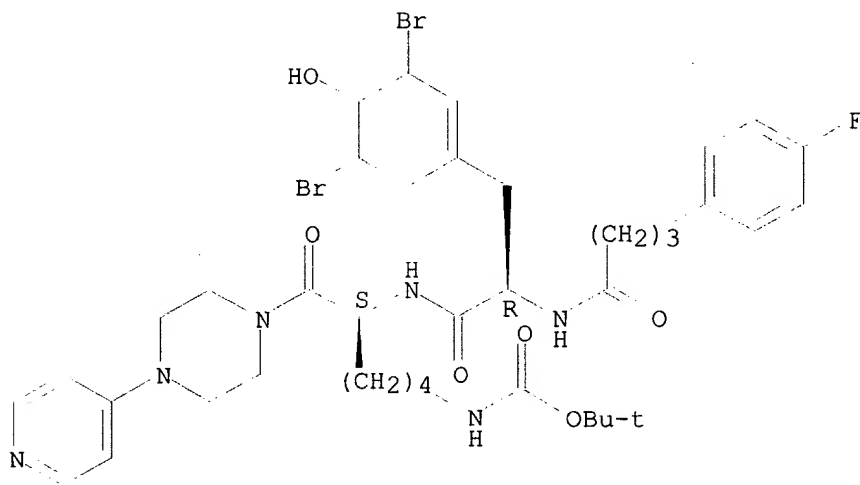
— Absolute stereochemistry.



RN 204698-27-1 CAPLUS

CN Carbamic acid, [5-[[3-(3,5-dibromo-4-hydroxyphenyl)-2-[[4-(4-fluorophenyl)-1-oxobutyl]amino]-1-oxopropyl]amino]-6-oxo-6-[4-(4-pyridinyl)-1-piperazinyl]hexyl]-, 1,1-dimethylethyl ester, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

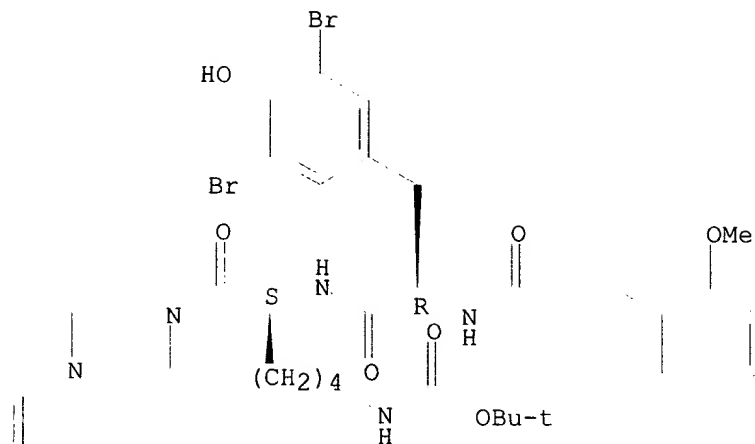
Absolute stereochemistry.



RN 204698-31-7 CAPLUS

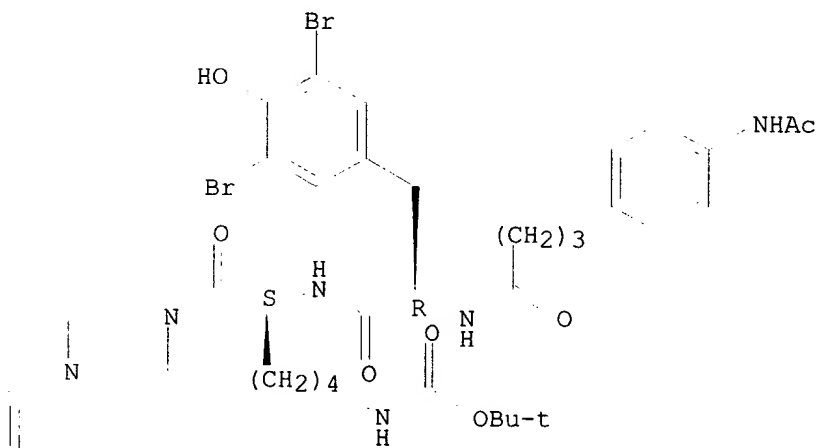
CN Carbamic acid, [5-[[3-(3,5-dibromo-4-hydroxyphenyl)-2-[[3-(2-methoxyphenyl)-1-oxopropyl]amino]-1-oxopropyl]amino]-6-oxo-6-[4-(4-pyridinyl)-1-piperazinyl]hexyl]-, 1,1-dimethylethyl ester, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204698-33-9 CAPLUS
 CN Carbamic acid, [5-[[2-[[4-(4-(acetamino)phenyl)-1-oxobutyl]amino]-3-(3,5-dibromo-4-hydroxyphenyl)-1-oxopropyl]amino]-6-oxo-6-[4-(4-pyridinyl)-1-piperazinyl]hexyl]-, 1,1-dimethylethyl ester, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



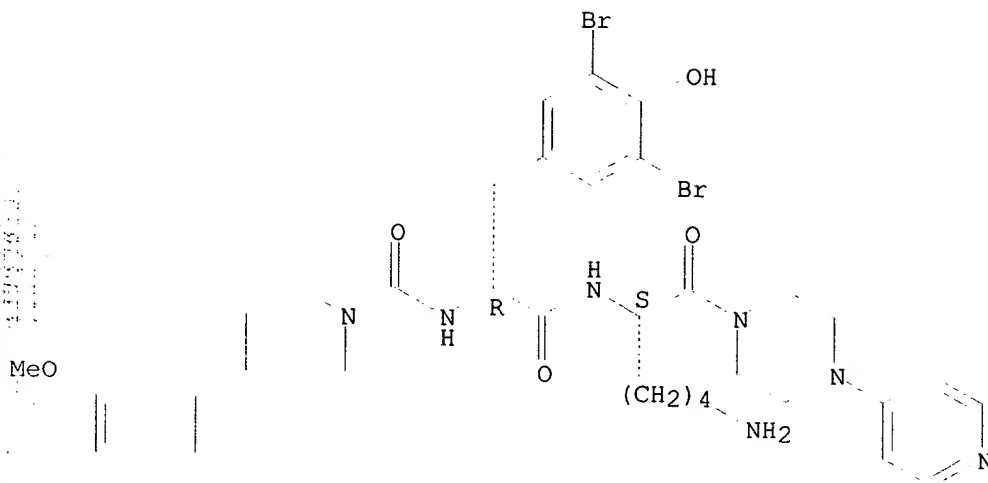
RN 204698-34-0 CAPLUS
 CN Carbamic acid, [5-[[2-[[4-(4-bromophenyl)-1-oxobutyl]amino]-3-(3,5-dibromo-4-hydroxyphenyl)-1-oxopropyl]amino]-6-oxo-6-[4-(4-pyridinyl)-1-piperazinyl]hexyl]-, 1,1-dimethylethyl ester, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

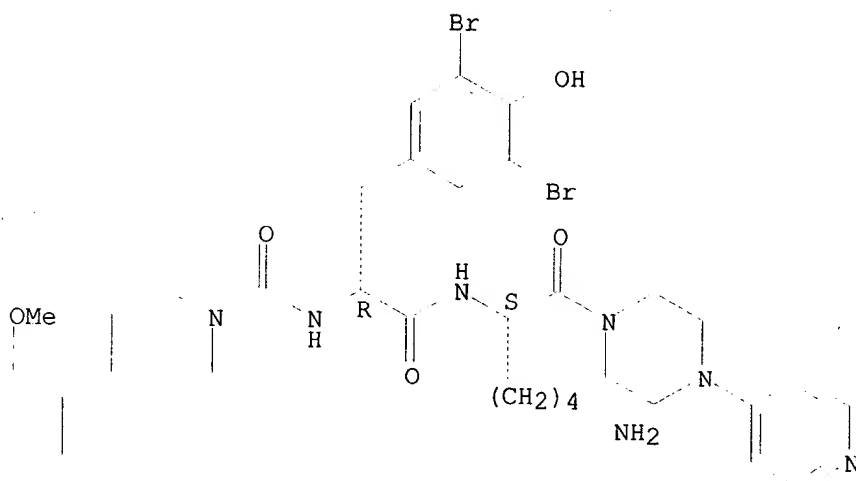
RN	204698-41-9	CAPLUS
CN	1(2H)-Pyridinecarboxamide, N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-3,6-dihydro-4-(3-methoxyphenyl)-, [R-(R*,S*)]-(9CI) (CA INDEX NAME)	

Absolute stereochemistry.



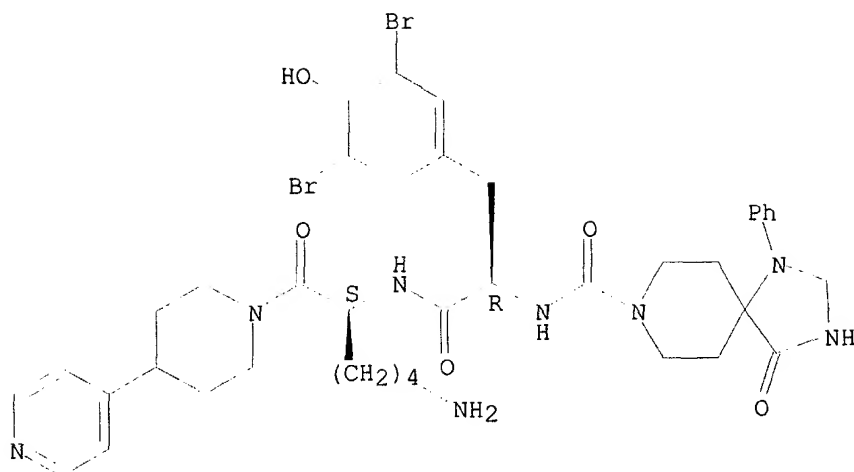
RN 204698-42-0 CAPLUS
 CN 1(2H)-Pyridinecarboxamide, N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-3,6-dihydro-4-(2-methoxyphenyl)-, [R-(R*,S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204698-44-2 CAPLUS
 CN 1,3,8-Triazaspiro[4.5]decane-8-carboxamide, N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperidinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-4-oxo-1-phenyl-, [R-(R*,S*)]]- (9CI) (CA INDEX NAME)

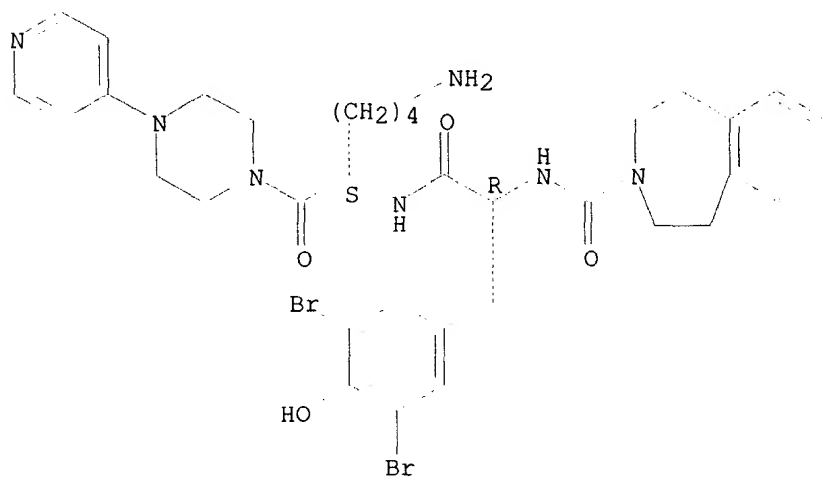
Absolute stereochemistry.



RN 204698-94-2 CAPLUS

CN 3H-3-Benzazepine-3-carboxamide, N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-1,2,4,5-tetrahydro-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L25 ANSWER 25 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:20532 CAPLUS

DOCUMENT NUMBER: 128:149915

TITLE: Proadrenomedullin N-terminal 20 peptide inhibits aldosterone secretion of human adrenocortical and Conn's adenoma cells: comparison with adrenomedullin effect

AUTHOR(S): Andreis, P. G.; Tortorella, C.; Mazzocchi, G.; Nussdorfer, G. G.

CORPORATE SOURCE: Department of Anatomy, University of Padua, Padua, I-35121, Italy

SOURCE: Journal of Clinical Endocrinology and Metabolism (1998), 83(1), 253-257

CODEN: JCEMAZ; ISSN: 0021-972X

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

Searched by Barb O'Bryen, STIC 308-4291

LANGUAGE:

English

AB Adrenomedullin (ADM) and proadrenomedullin N-terminal 20 peptide (PAMP) are two vasoactive peptides, which are highly expressed in human adrenal gland. Autoradiog. showed the presence of abundant [125I]ADM and [125I]PAMP binding sites in both the outer cortex and medulla of human adrenals. ADM, but not PAMP binding was completely displaced by the specific CGRP1 receptor antagonist CGRP(8-37). ADM and PAMP concn.-dependently inhibited angiotensin-II (ANG-II)-stimulated, but not basal aldosterone secretion of dispersed human adrenocortical cells. PAMP was significantly more potent than ADM (IC₅₀, 0.98 .times. 10⁻¹¹ vs. 3.16 .times. 10⁻⁹ mol/L). CGRP(8-37) abolished the inhibitory action of ADM, without affecting that of PAMP. Qual. analogous findings were obtained using aldosteronoma dispersed cells. However, tumor cells were more sensitive than normal adrenocortical cells (IC₅₀ were 1.32 .times. 10⁻¹² and 1.51 .times. 10⁻⁹ mol/L for PAMP and ADM, resp.). Moreover, PAMP was found to also depress basal aldosterone secretion (IC₅₀, 4.27 .times. 10⁻¹¹ mol/L). Neither basal nor ANG-II-stimulated cortisol prodn. by both normal and tumorous adrenocortical cells was altered by ADM or PAMP. Collectively, these findings confirm that ADM (CGRP1) and PAMP receptors are present in the human outer adrenal cortex and allow us to draw the following conclusions: (1) because of its potency, PAMP may a better candidate for being considered a physiol. regulator of aldosterone secretion than ADM; and (2) under pathol. conditions, both peptides may be capable of reversing overprodn. of aldosterone.

IT 150238-87-2, Human PAMP

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

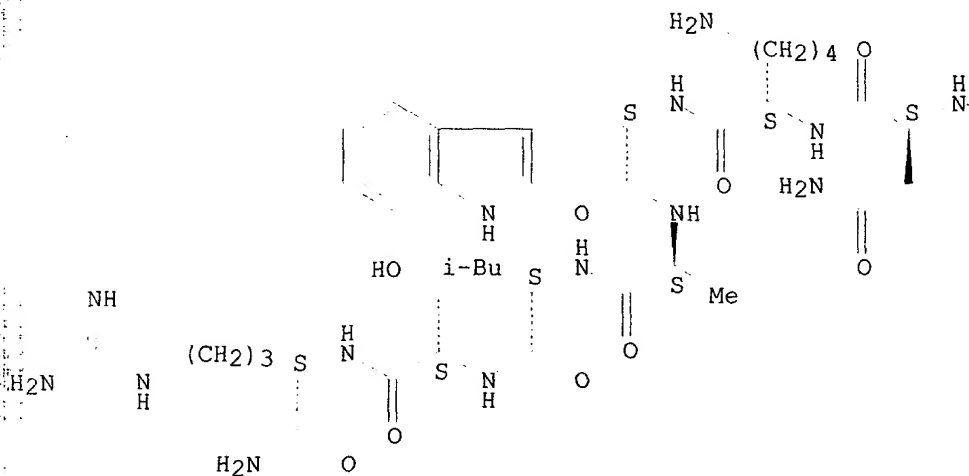
(proadrenomedullin N-terminal 20 peptide and adrenomedullin inhibition of aldosterone secretion in human adrenocortical and Conn's adenoma cells)

RN 150238-87-2 CAPLUS

CN L-Argininamide, L-alanyl-L-arginyl-L-leucyl-L-.alpha.-aspartyl-L-valyl-L-alanyl-L-seryl-L-.alpha.-glutamyl-L-phenylalanyl-L-arginyl-L-lysyl-L-lysyl-L-tryptophyl-L-asparaginy-L-lysyl-L-tryptophyl-L-alanyl-L-leucyl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



Chemical structure of a polythiobenzamide chain, showing various side chains (R, (CH₂)₃, Ph, Me, Pr-i, Bu-i, CO₂H) and stereochemistry.

CCCCNC(=N)N
$$\begin{array}{c} \text{R}^2 \\ \vdots \\ \text{HN} \cdots \text{C}(=\text{O}) \cdots \text{S}(\text{R}) \cdots (\text{CH}_2)_4 \text{NH}_2 \end{array}$$

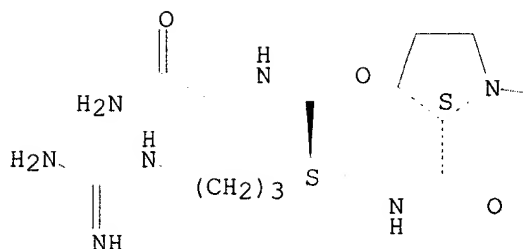
125 ANSWER 26 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:738241 CAPLUS
DOCUMENT NUMBER: 128:43625
TITLE: Effects of SR 49059, a new orally active and specific
vasopressin V1 receptor antagonist, on
vasopressin-induced vasoconstriction in humans
AUTHOR(S): Weber, Roger; Pechere-Bertschi, Antoinette; Hayoz,
Daniel; Gerc, Vjekoslav; Brouard, Remi; Lahmy,
Jean-Paul; Brunner, Hans R.; Burnier, Michel
CORPORATE SOURCE: Division of Hypertension and Vascular Medicine,
Lausanne, 1011, Switz.
SOURCE: Hypertension (Dallas) (1997), 30(5), 1121-1127
CODEN: HPRTDN; ISSN: 0194-911X
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have evaluated the efficacy of SR 49059, a new orally active and specific vasopressin V1 receptor antagonist (arginine-vasopressin [AVP]), in the blockade of the vascular effects of exogenous AVP in healthy subjects. In preliminary expts., two procedures to measure the V1 vascular effects of AVP were assessed. First, the AVP-induced changes in skin blood flow were investigated by the injection of increasing doses of AVP intradermally, with or without a previous local vasodilation with calcitonin gene-related peptide (CGRP). In a second protocol, AVP was infused intra-arterially, and the changes in radial artery diam. and blood flow were measured. The intradermal injection of AVP caused significant decreases in skin blood flow, and the use of CGRP increased the sensitivity of the method by a factor of 102 to 103. AVP infused intra-arterially caused dose-dependent decreases in the radial artery diam. and blood flow. In the main study, the potency and efficacy of SR 49059 to block the AVP-induced changes in skin blood flow were assessed in 12 healthy men with a double-blind, triple crossover study design. The subjects were randomized to receive a placebo orally and 30 mg and 300 mg of the antagonist at a 1-wk interval. The subjects were then further randomized to evaluate the efficacy of the same doses of the antagonist to block the vasoconstriction of the radial artery induced by an intra-arterial infusion of AVP. SR 49059 inhibits, dose-dependently and significantly, the AVP-induced changes in skin blood flow, with a peak effect occurring between 2 and 6 h after injection. In addn., the 300-mg dose of SR 49059 completely blocked the vasoconstriction of the radial artery induced by AVP. In conclusion, skin blood-flow measurement, after intradermal injection of AVP on a skin area vasodilated with CGRP, is an effective method to investigate the V1 vascular effect of AVP in humans. SR 49059 is a potent and specific antagonist of V1 receptors, which blocks the AVP-induced vasoconstriction.

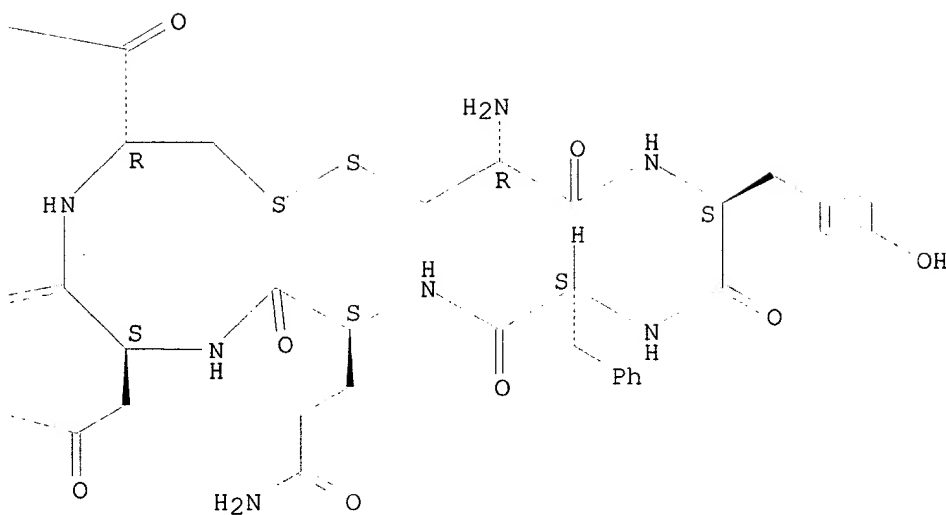
IT 113-79-1, Arginine vasopressin
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); BIOL (Biological study)
(effects of SR 49059, orally active and specific vasopressin V1
receptor antagonist, on vasopressin-induced
vasoconstriction in humans)
RN 113-79-1 CAPLUS
CN Vasopressin, 8-L-arginine- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



IT 150375-75-0, SR 49059

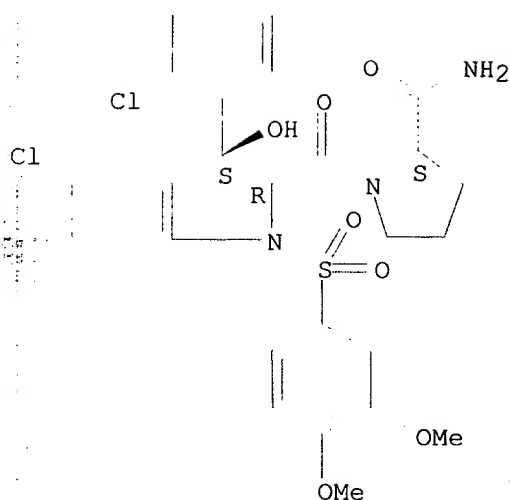
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effects of SR 49059, orally active and specific vasopressin V1 receptor antagonist, on vasopressin-induced vasoconstriction in humans)

RN 150375-75-0 CAPLUS

CN 2-Pyrrolidinecarboxamide, 1-[[(2R,3S)-5-chloro-3-(2-chlorophenyl)-1-[(3,4-dimethoxyphenyl) sulfonyl]-2,3-dihydro-3-hydroxy-1H-indol-2-yl]carbonyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L25 ANSWER 27 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:555710 CAPLUS

DOCUMENT NUMBER: 127:243560

TITLE: Proadrenomedullin N-terminal 20 peptide (PAMP)
inhibits proliferation of human neuroblastoma TGW
cells

AUTHOR(S): Ando, Katsuyuki; Omi, Naomi; Shimosawa, Tatsuo;
Fujita, Toshiro

CORPORATE SOURCE: Fourth Department of Internal Medicine, University of
Tokyo School of Medicine, 3-28-6 Mejirodai, Bunkyo-ku,
Tokyo, 112, Japan

SOURCE: FEBS Letters (1997), 413(3), 462-466

CODEN: FEBLAL; ISSN: 0014-5793

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors investigated the effects of proadrenomedullin N-terminal 20
peptide (PAMP) and adrenomedullin (AM) on the growth of human
neuroblastoma TGW cells. Both PAMP and AM inhibited growth and DNA
synthesis in neuroblastoma cells. Calcitonin gene-related peptide
(CGRP)8-37, an antagonist to CGRP, abolished the inhibitory effect of AM
on growth and DNA synthesis of neuroblastoma cells but did not affect that
of PAMP. AM22-52, an antagonist to AM, also reversed the effect of AM.
Pertussis toxin (PTX) and .omega.-conotoxin GIVA blocked the effect of
PAMP alone. Thus, PAMP inhibits the growth of neuroblastoma cells by
inhibiting N-type Ca²⁺ channels through PTX-sensitive G protein-coupled
receptors, which is different mechanism of AM-induced inhibition of the
cell growth.

IT 150238-87-2, Human PAMP

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); BIOL (Biological study)

(proadrenomedullin N-terminal 20 peptide inhibits proliferation of
human neuroblastoma TGW cells)

RN 150238-87-2 CAPLUS

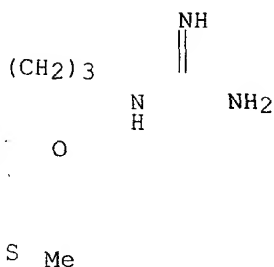
CN L-Argininamide, L-alanyl-L-arginyl-L-leucyl-L-.alpha.-aspartyl-L-valyl-L-
alanyl-L-seryl-L-.alpha.-glutamyl-L-phenylalanyl-L-arginyl-L-lysyl-L-lysyl-
L-tryptophyl-L-asparagyl-L-lysyl-L-tryptophyl-L-alanyl-L-leucyl-L-seryl-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

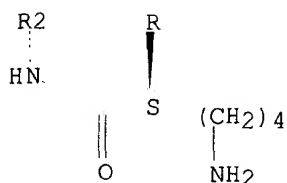
The chemical structure of the 12S peptide is shown, featuring a complex chain of amino acids and modified residues. Key features include a pyrrole ring, an isobutyl (i-Bu) group, a long-chain thioether ((CH₂)₄), and a terminal amine group (H₂N).

Chemical structure 1: A complex peptide derivative. The structure shows a central backbone with various side chains. Key features include a long $(CH_2)_3$ chain, a phenyl group (Ph), a methyl group (Me), and a butyl group ($Bu-i$). The structure includes amide bonds, a carboxylic acid group (CO_2H), and a thioether linkage (S). Stereochemistry is indicated with wedges and dashes.

PAGE 2-B



PAGE 3-A



L25 ANSWER 28 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:493910 CAPLUS

DOCUMENT NUMBER: 127:171754

TITLE: Modulation of synovial blood flow by the
**calcitonin gene-related
 peptide (CGRP) receptor
 antagonist, CGRP(8-37)**

AUTHOR(S): Mcmurdo, Lorraine; Lockhart, J.C.; Ferrell, W.R.

CORPORATE SOURCE: Institute of Biomedical & Life Sciences, University of
 Glasgow, Glasgow, G12 8QQ, UKSOURCE: British Journal of Pharmacology (1997), 121(6),
 1075-1080

CODEN: BJPCBM; ISSN: 0007-1188

PUBLISHER: Stockton

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of the calcitonin gene-related peptide (CGRP) receptor antagonist, CGRP(8-37) on blood flow in the knee joint of the anesthetized rat was investigated. Synovial blood flow in both exposed and intact, skin-covered knees was measured by laser Doppler perfusion imaging. Topical application of CGRP(8-37) caused a dose-dependent fall in synovial blood flow in the exposed knee joint of the rat. At low (1.5 nmol) doses of CGRP(8-37) there was no significant effect on synovial blood flow. In rats treated with 7.5 nmol CGRP(8-37) there was a fall in synovial blood flow (max. effect at 10 min: -28.8%), which returned to resting levels within 30 min. The highest dose (15 nmol) of antagonist used in this study caused a marked (max. at 10 min: -35.6%), and prolonged (up to 30 min) fall in blood flow. Ten days after surgical denervation, CGRP(8-37) (15 nmol, topical) had no significant effect on blood flow in the rat exposed knee joint (change in flux at 10 min: -5.1%). This suggests that CGRP(8-37) acts selectively to antagonize the actions of a neurally derived product, probably CGRP, on the rat synovial vasculature. In skin-covered knee joints, intra-articular injection of CGRP(8-37) (15 nmol; bolus) elicited a significant fall in synovial blood flow (max. effect at 10 min: -15.5%). CGRP (0.01, 0.1 or 1.0 nmol; topical) caused a dose-dependent increase in exposed knee joint blood flow, which was

attenuated by co-administration of 1.5 nmol CGRP(8-37). For example, 1 nmol CGRP elicited a peak increase in flux at 10 min of 94.7% and 28.8% in the absence and presence of CGRP(8-37), resp. The vasodilator responses induced by acetylcholine (ACh) (10 nmol, topical; -5) or sodium nitroprusside (SNP) (10 nmol, topical; -5) were unaltered in the presence of CGRP(8-37) (1.5 nmol, topical). Thus, the CGRP receptor antagonist CGRP(8-37) elicits vasoconstriction in the rat synovium. This suggests that the endogenous, basal release of CGRP may play a physiol. role in the regulation of blood flow in the rat knee joint.

IT 119911-68-1, Human CGRP(8-37)

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); BIOL (Biological study)

(modulation of synovial blood flow by the calcitonin

gene-related peptide (CGRP)

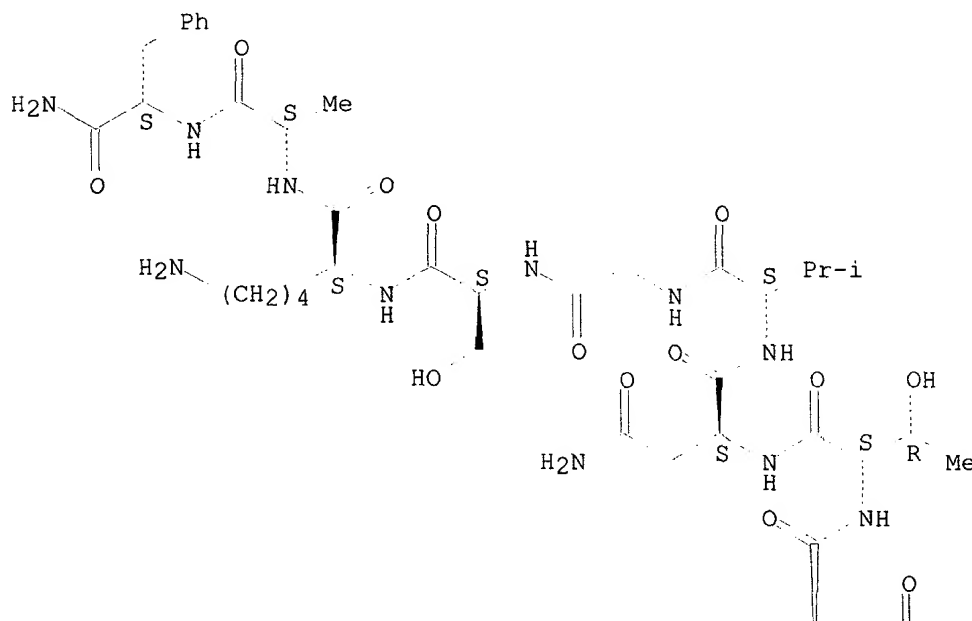
receptor antagonist, CGRP(8-37))

RN 119911-68-1 CAPLUS

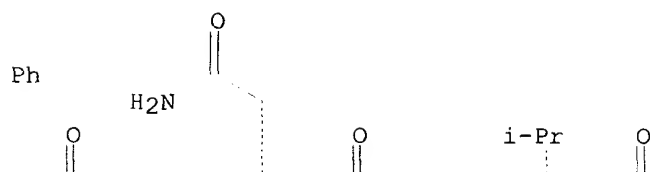
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



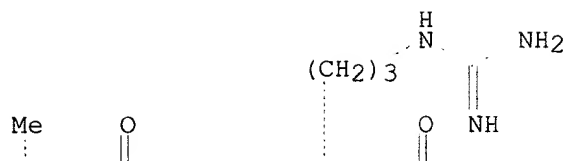
PAGE 1-B



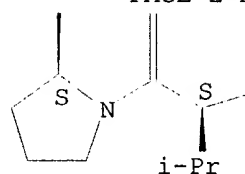
PAGE 1-C



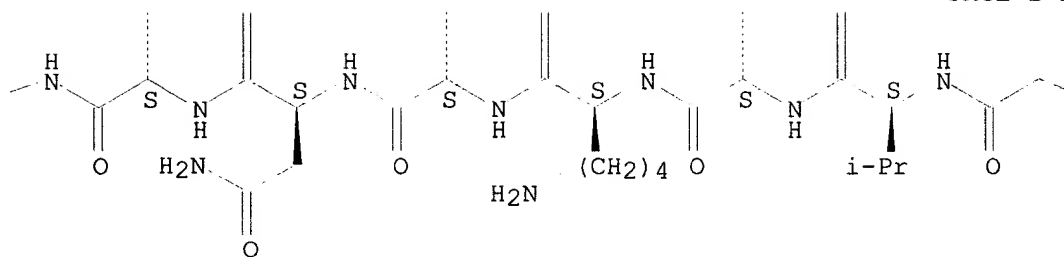
PAGE 1-D



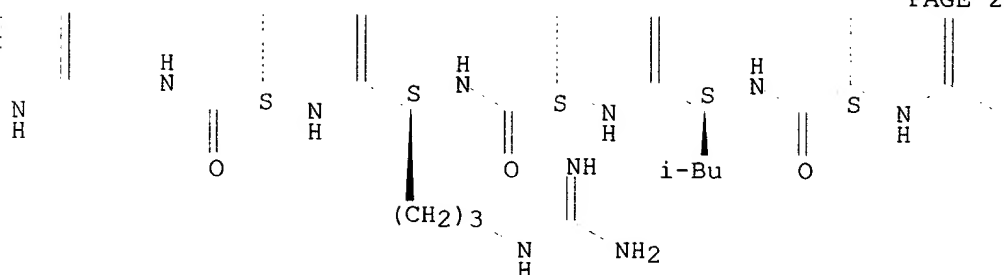
PAGE 2-A



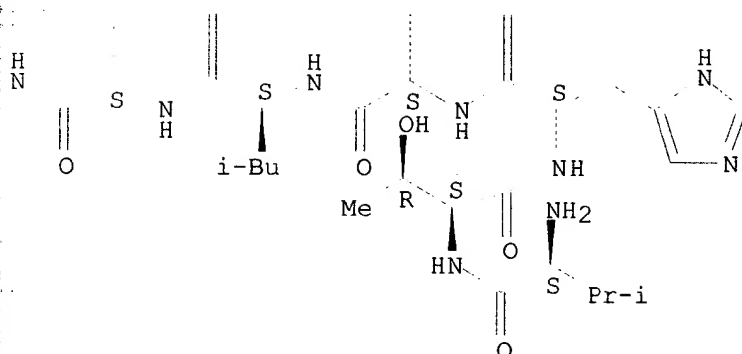
PAGE 2-B



PAGE 2-C



PAGE 2-D



L25 ANSWER 29 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:459118 CAPLUS

DOCUMENT NUMBER: 127:156846

TITLE: The selectivity and structural determinants of peptide antagonists at the CGRP receptor of rat, L6 myocytes

AUTHOR(S) : Howitt, Stephen G.; Poyner, David R.

2. CORPORATE SOURCE: Rowles, Stephen G.; Poyner, David R.
Department of Pharmaceutical and Biological Sciences,
Aston University, Birmingham, B4 7ET, UK

SOURCE: British Journal of Pharmacology (1997), 121(5), 1000-1004

CODEN: BJPCBM; ISSN: 0007-1188

.PUBLISHER: Stockton

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Potency orders were detd. for a series of agonists and antagonists on the calcitonin gene-related peptide (CGRP) receptor of rat L6 myocytes. The agents tested were all shown to have been active against CGRP, amylin or adrenomedullin receptors. AC187 had a pIC50 of 6.8, making it 14-fold less potent as an antagonist than CGRP8-37 (pIC50, 7.95). Amylin8-37 was equipotent to AC187 (pIC50, 6.6) and CGRP19-37 was 3-fold less potent than either (pIC50, 6.1). [Ala11]-CGRP8-37 was 6-fold less potent than CGRP8-37, (pIC50, 7.13), whereas [Ala18]-CGRP8-37 was approx. equipotent to CGRP8-37 (pIC50, 7.52). However, [Ala11,Ala18]-CGRP8-37 was over 300-fold less potent than CGRP8-37 (pIC50, 5.30). [Tyr0]-CGRP28-37, amylin19-37 and adrenomedullin22-52 were inactive as antagonists at concns. of up to 1 .mu.M. Biotinyl-human .alpha.-CGRP was 150-fold less potent than human .alpha.-CGRP itself (EC50 values of 48 nM and 0.31 nM, resp.). At 1 .mu.M, [Cys(acetomethoxy)2,7]-CGRP was inactive as an agonist. These results confirm a role for Arql1 in maintaining the high

affinity binding of CGRP8-37. Arg18 is of less direct significance for high affinity binding, but it may be important in maintaining the amphipathic nature of CGRP and its analogs.

IT 119911-68-1, 8-37-.alpha.-Calcitonin gene-related peptide (human) 129693-73-8
141017-72-3 159899-65-7, Human adrenomedullin22-52
193549-53-0 193549-55-2 193549-59-6
193549-63-2

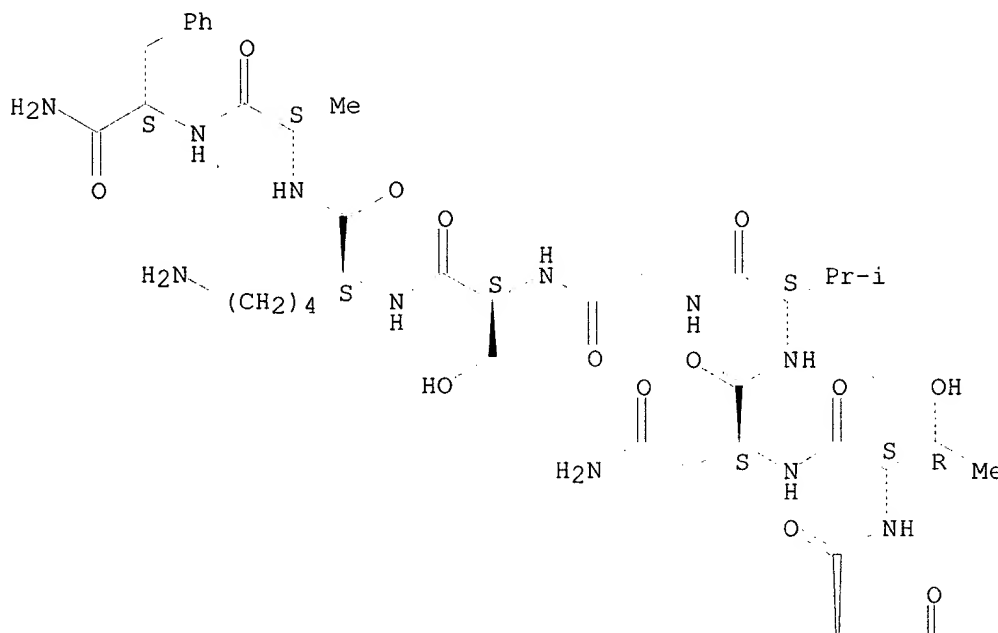
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(the selectivity and structural determinants of peptide antagonists at the CGRP receptor of rat L6 myocytes)

RN 119911-68-1 CAPLUS

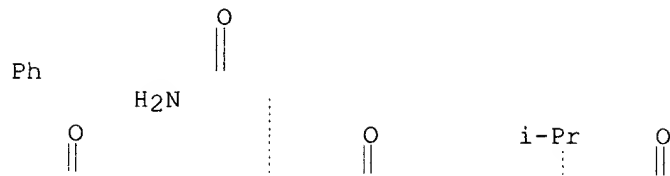
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



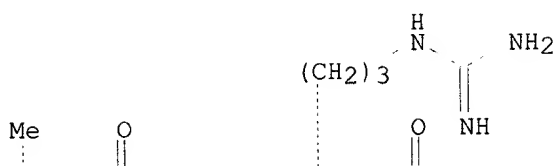
PAGE 1-B



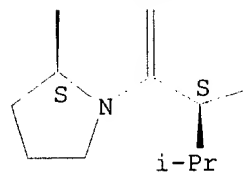
PAGE 1-C



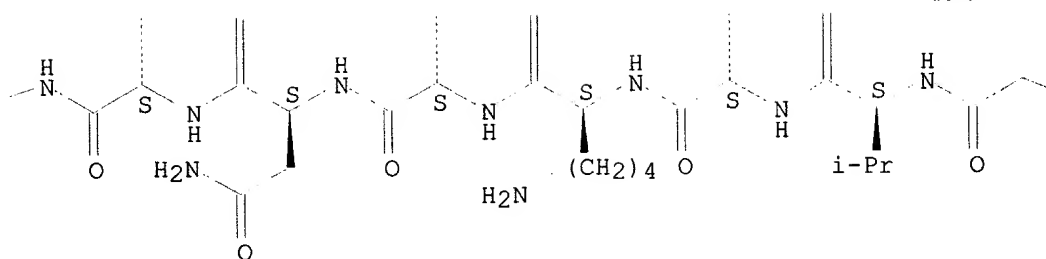
PAGE 1-D

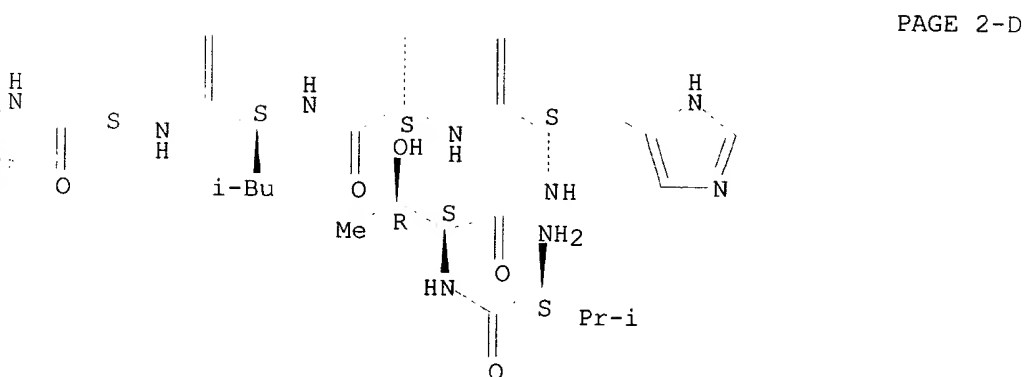
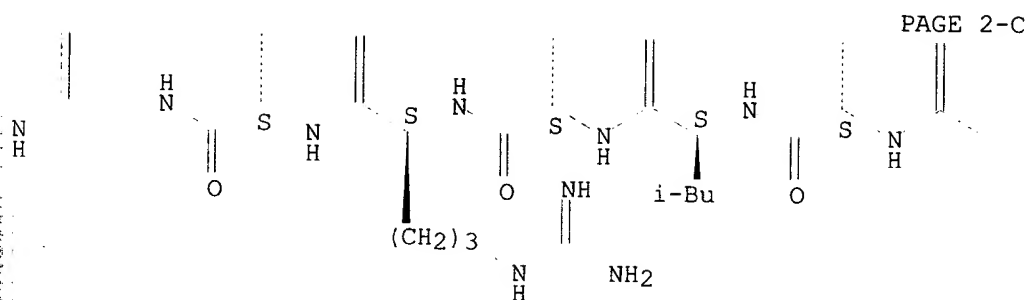


PAGE 2-A



PAGE 2-B

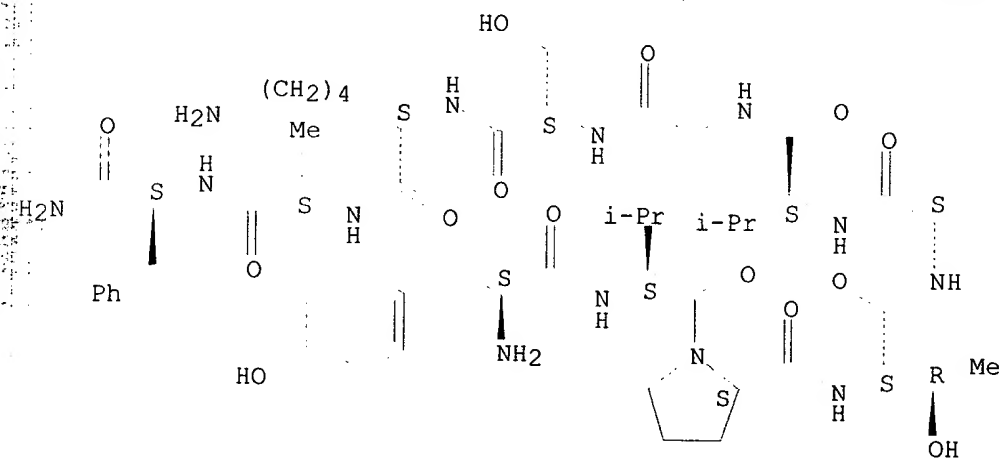




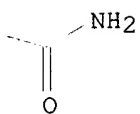
RN 129693-73-8 CAPLUS
 CN L-Phenylalaninamide, L-tyrosyl-L-valyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-lysyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



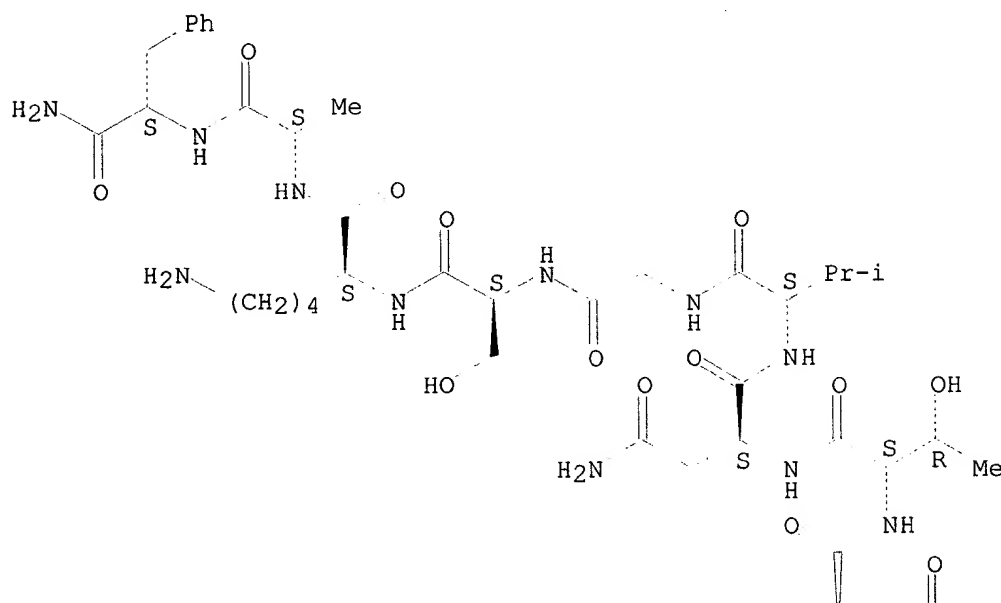
PAGE 1-B



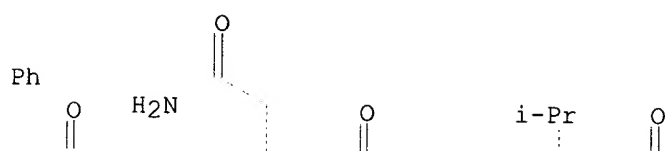
RN	141017-72-3	CAPLUS
CN	.alpha.-Calcitonin gene-related peptide (human reduced), 1-de-L-alanine-2-de-L-cysteine-3-de-L-aspartic acid-4-de-L-threonine-5-de- L-alanine-6-de-L-threonine-7-de-L-cysteine-11-L-alanine- (9CI) (CA INDEX NAME)	

Absolute stereochemistry.

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PAGE 1-B



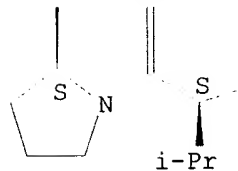
PAGE 1-C



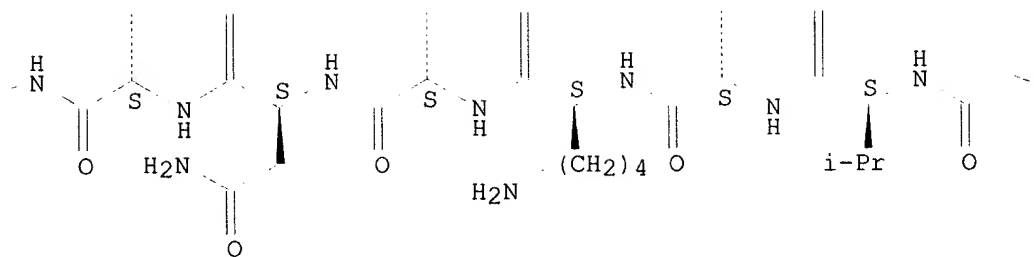
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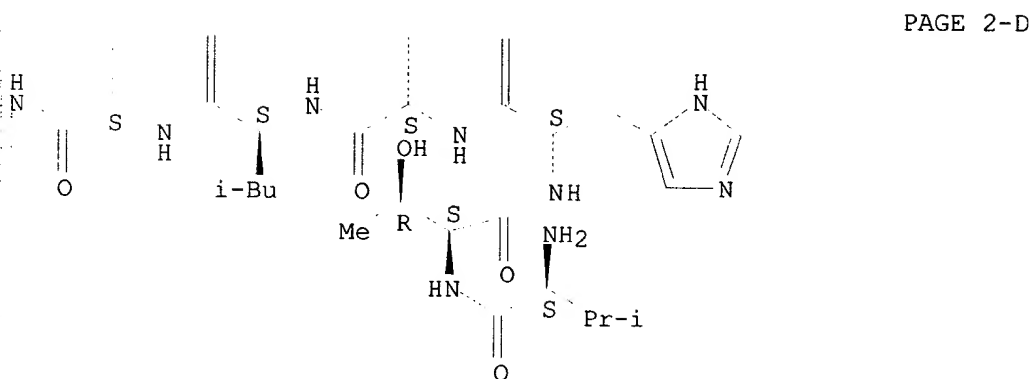
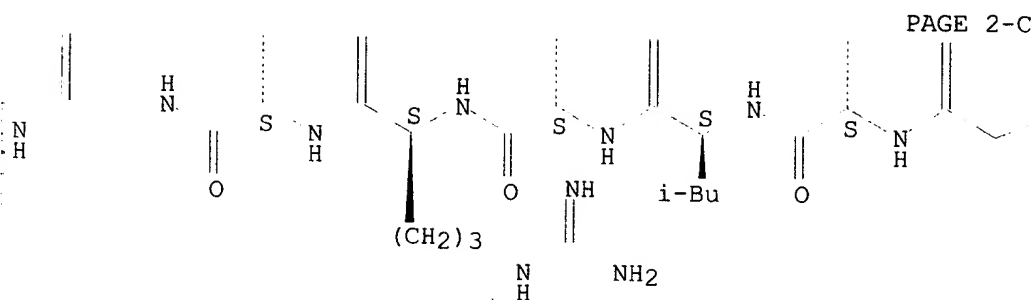


PAGE 2-A



PAGE 2-B



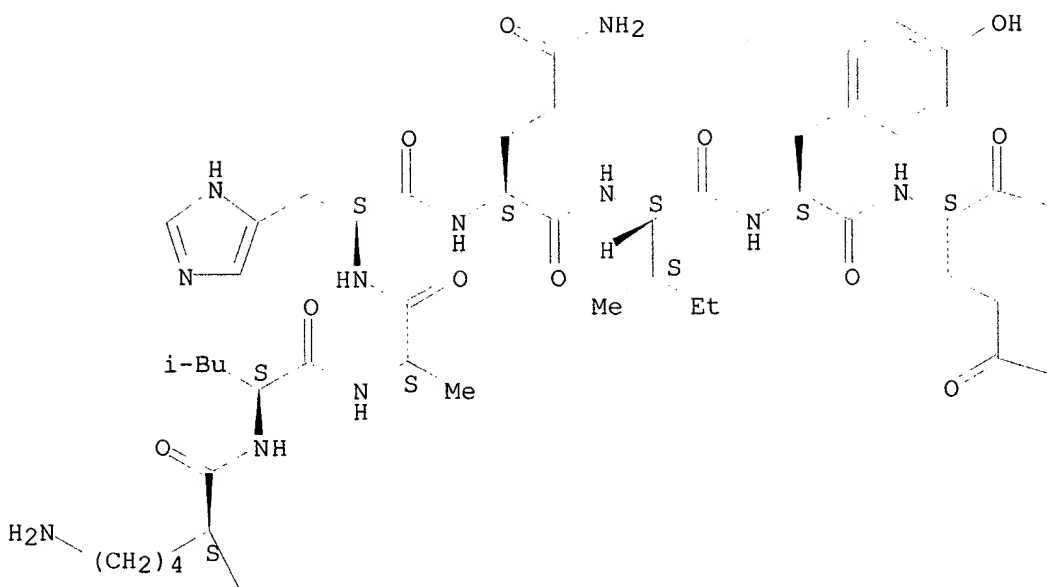


159899-65-7 CAPLUS

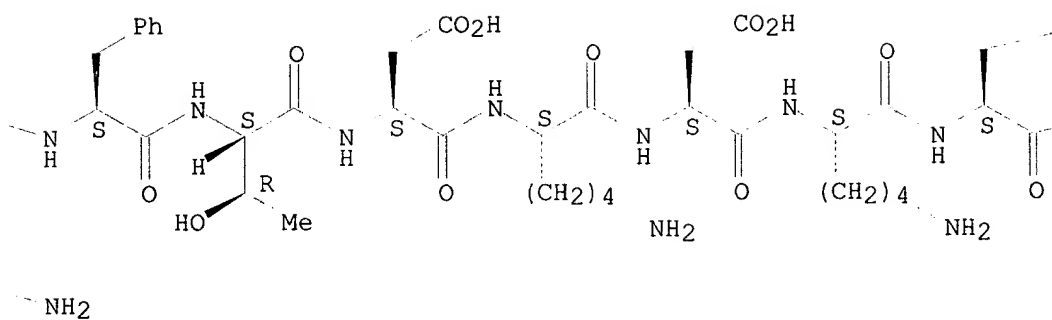
L-Tyrosinamide, L-threonyl-L-valyl-L-glutaminyl-L-lysyl-L-leucyl-L-alanyl-L-histidyl-L-glutaminyl-L-isoleucyl-L-tyrosyl-L-glutaminyl-L-phenylalanyl-L-threonyl-L-.alpha.-aspartyl-L-lysyl-L-.alpha.-aspartyl-L-lysyl-L-.alpha.-aspartyl-L-asparaginyl-L-valyl-L-alanyl-L-prolyl-L-arginyl-L-seryl-L-lysyl-L-isoleucyl-L-seryl-L-prolyl-L-glutaminylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

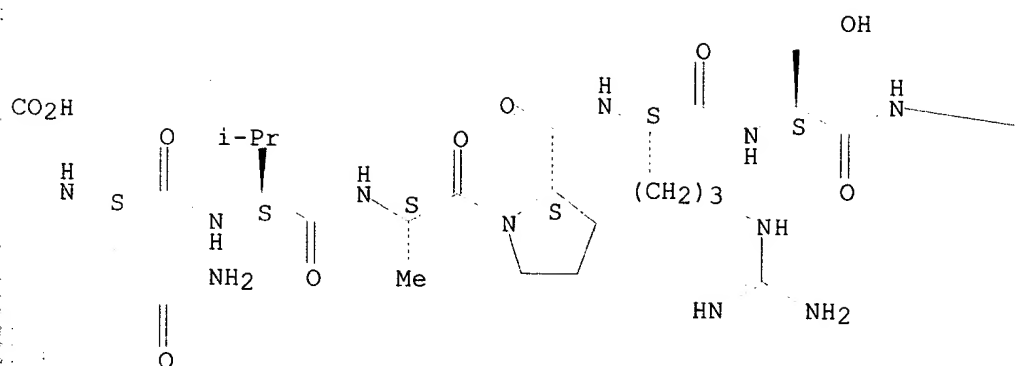
PAGE 1-A



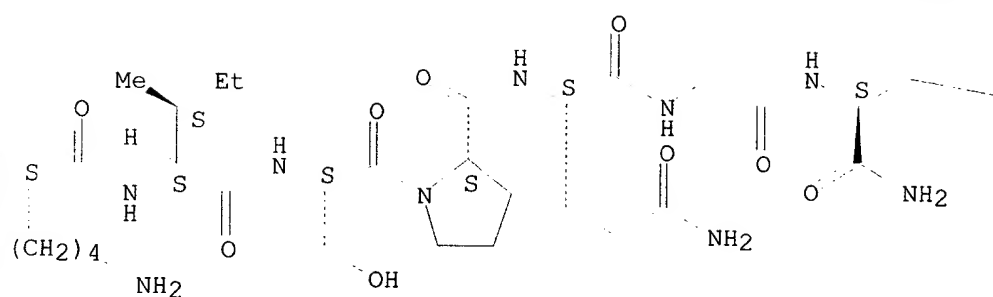
PAGE 1-B



PAGE 1-C



PAGE 1-D

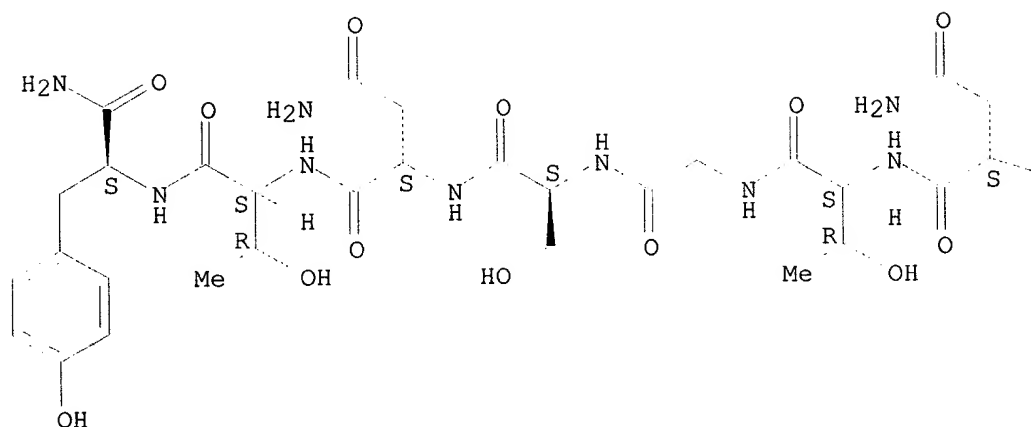


PAGE 1-E

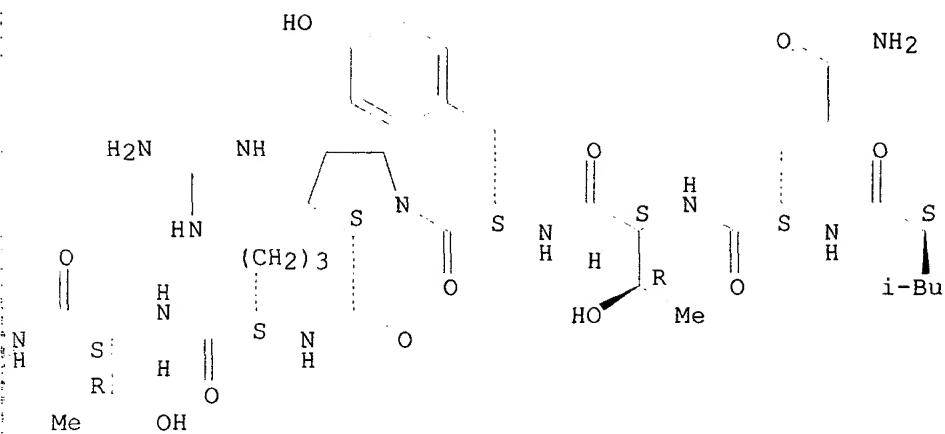
OH

Absolute stereochemistry.

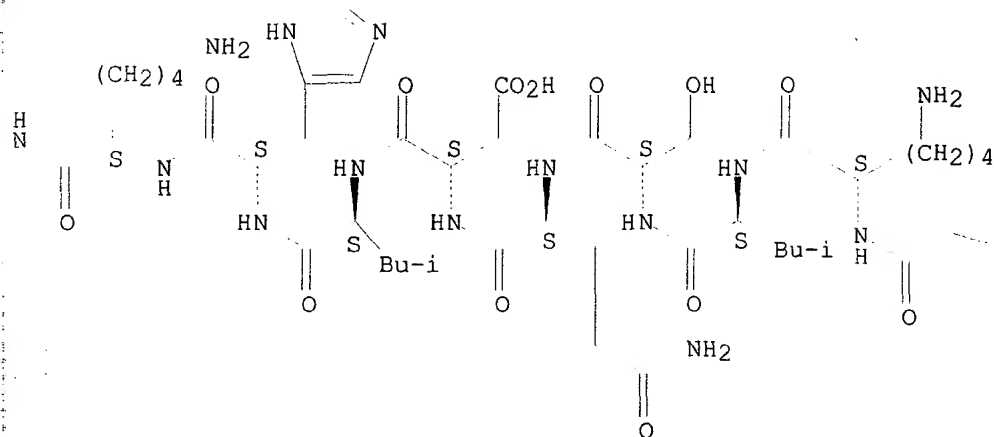
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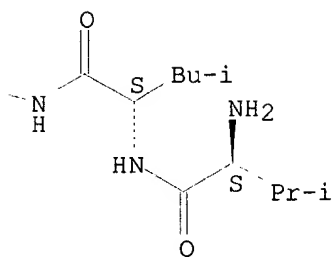
PAGE 1-B



PAGE 1-C



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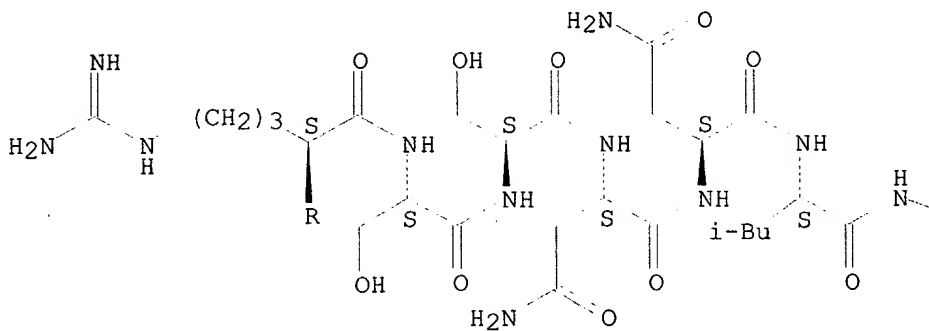


RN 193549-55-2 CAPLUS

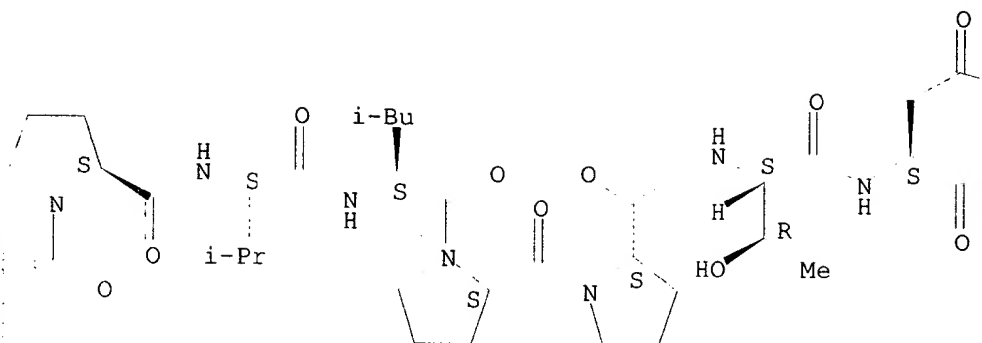
CN L-Tyrosinamide, L-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-arginyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-leucylglycyl-L-prolyl-L-valyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-alanyl-L-asparaginyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

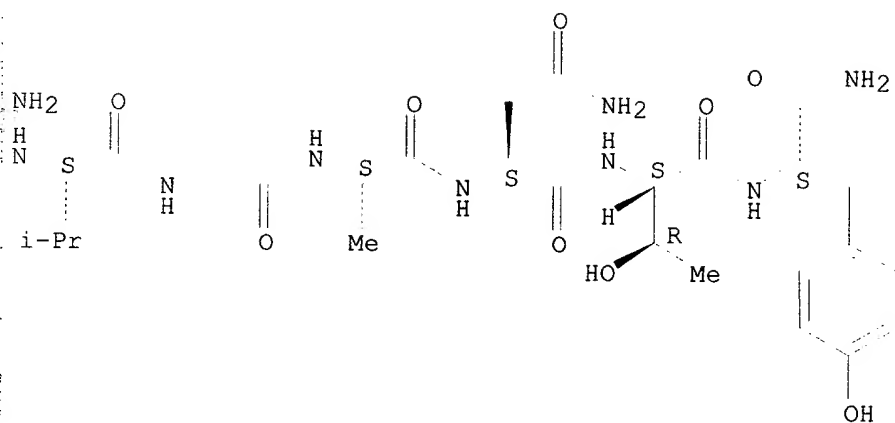
PAGE 1-A



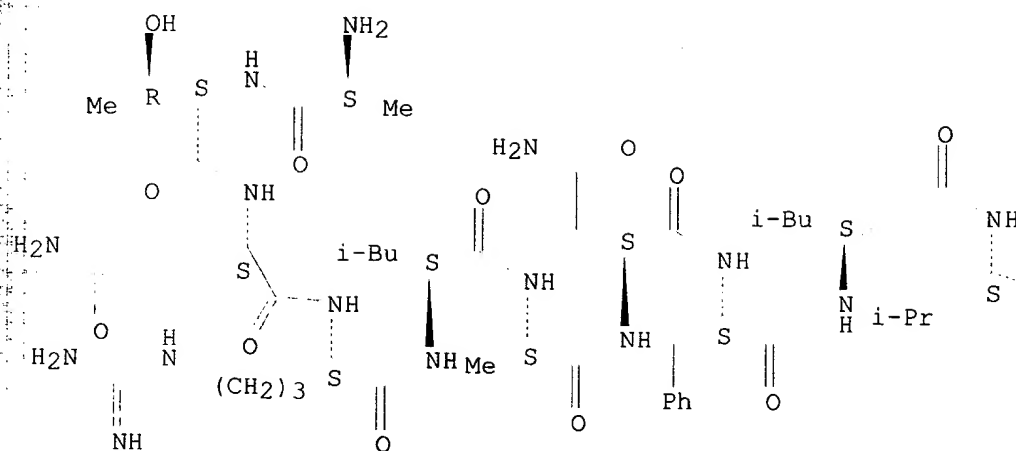
PAGE 1-B



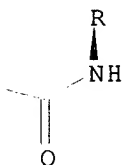
PAGE 1-C



PAGE 2-A



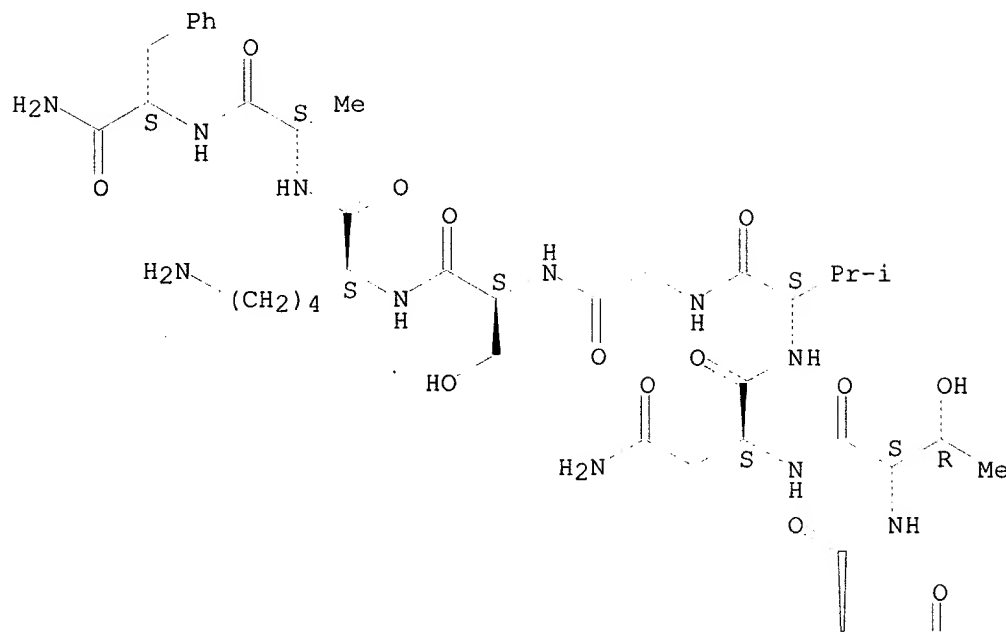
PAGE 2-B



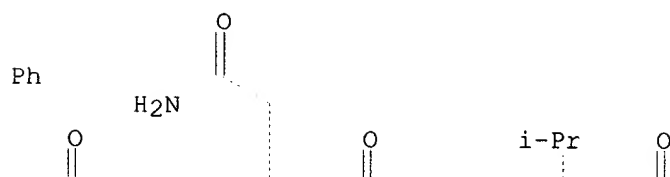
RN 193549-59-6 CAPLUS
CN 8-37-.alpha.-Calcitonin gene-related peptide (human reduced),
18-L-alanine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



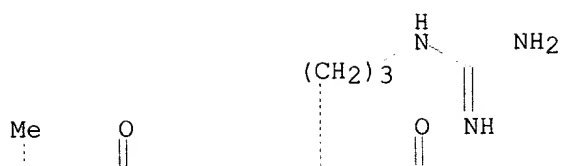
PAGE 1-B



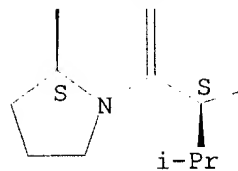
PAGE 1-C



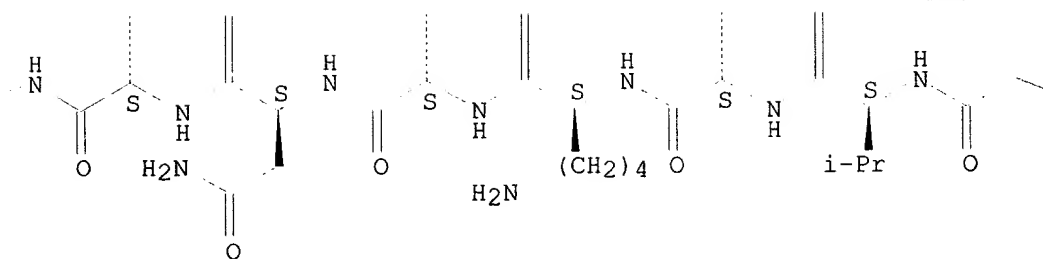
PAGE 1-D



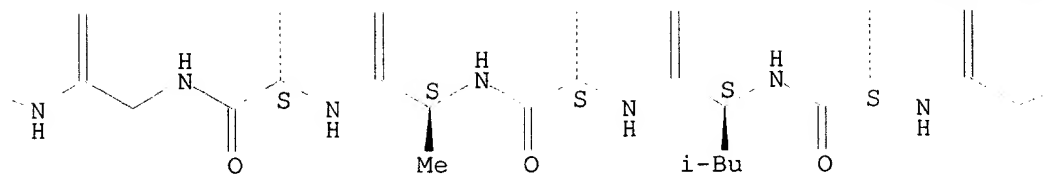
PAGE 2-A



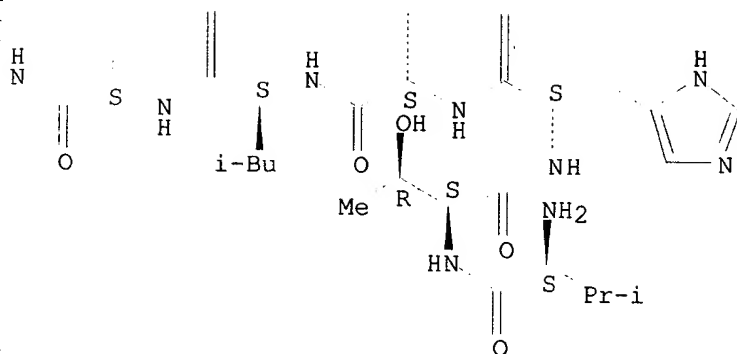
PAGE 2-B



PAGE 2-C



PAGE 2-D

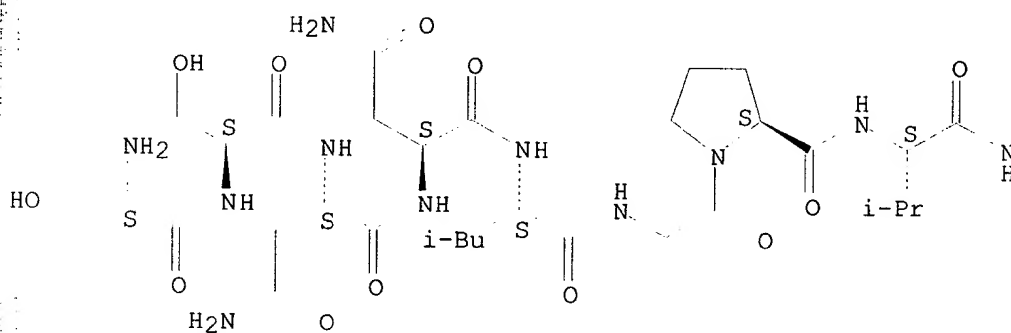


193549-63-2 CAPLUS

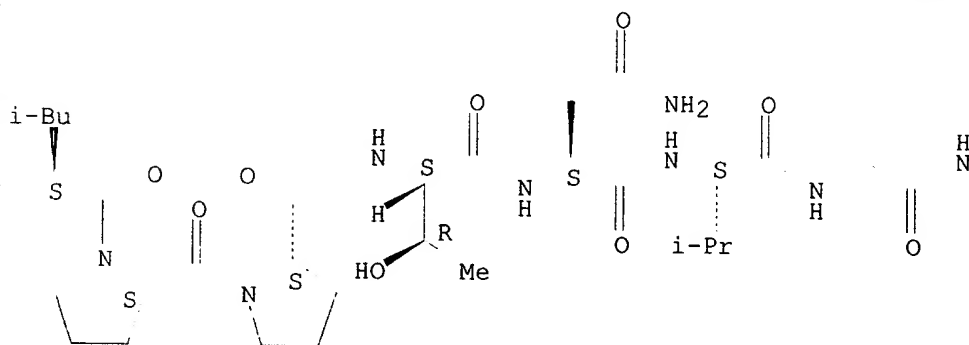
L-Tyrosinamide, L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-leucylglycyl-L-prolyl-L-valyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-alanyl-L-asparaginyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

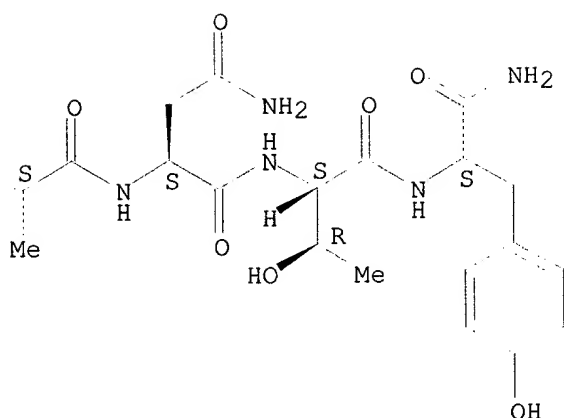
PAGE 1-A



PAGE 1-B



PAGE 1-C



L25 ANSWER 30 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:417932 CAPLUS

DOCUMENT NUMBER: 127:117656

TITLE: Different influence of **CGRP** (8-37), an amylin and **CGRP antagonist**, on the anorectic effects of cholecystokinin and bombesin in diabetic and normal rats

AUTHOR(S): Lutz, T. A.; Pieber, T. R.; Walzer, B.; Del Prete, E.; Scharrer, E.

CORPORATE SOURCE: Institute Veterinary Physiology, University Zuerich, Zurich, CH 8057, Switz.

SOURCE: Peptides (Tarrytown, New York) (1997), 18(5), 643-649
CODEN: PPTDD5; ISSN: 0196-9781

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Because previous studies had suggested that the anorectic effects of cholecystokinin (CCK) and bombesin (BBS) depend partly on the release of amylin or calcitonin gene-related peptide (CGRP), we investigated the influence of the amylin and CGRP receptor antagonist CGRP (8-37) on the anorectic effects of CCK and BBS in streptozotocin (STZ)-diabetic and nondiabetic rats. STZ-diabetic rats had significantly lower plasma amylin and insulin concns. than nondiabetic control rats. Amylin (5 .mu.g/kg or 2.5 .mu.g/kg) injected i.p. at dark onset after 24-h food deprivation elicited an anorectic effect of similar extent in STZ-diabetic and control rats. Under similar conditions, CCK (0.25 and 2 .mu.g/kg) and BBS (5 .mu.g/kg) reduced food intake in both STZ-diabetic and nondiabetic rats. These effects were markedly attenuated by CGRP (8-37) (10 .mu.g/kg) in nondiabetics but not in STZ-diabetic rats. It is concluded that part of the anorectic effects of CCK and BBS depend on the release of amylin from pancreatic B-cells.

IT 31362-50-2, Bombesin

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); BIOL (Biological study)

(amylin and **CGRP antagonist** effect on anorectic

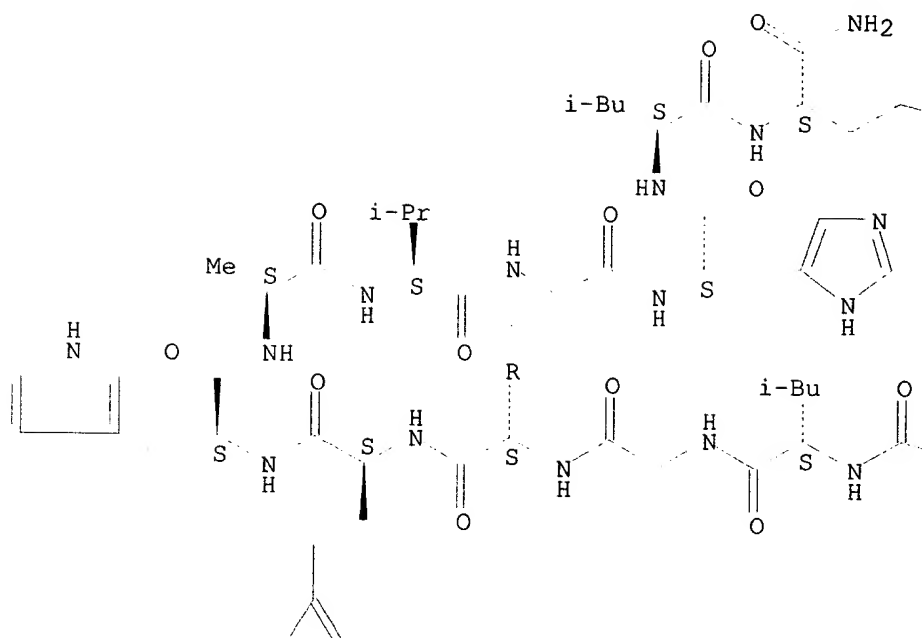
effects of cholecystokinin and bombesin in diabetic and normal rats)

RN 31362-50-2 CAPLUS

CN Bombesin (9CI) (CA INDEX NAME)

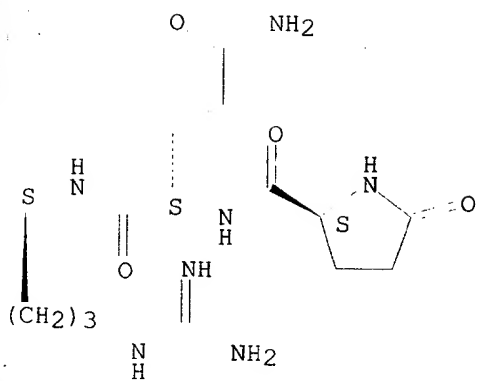
Absolute stereochemistry.

PAGE 1-A

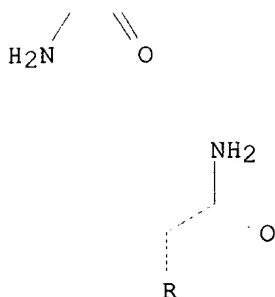


PAGE 1-B

SMe



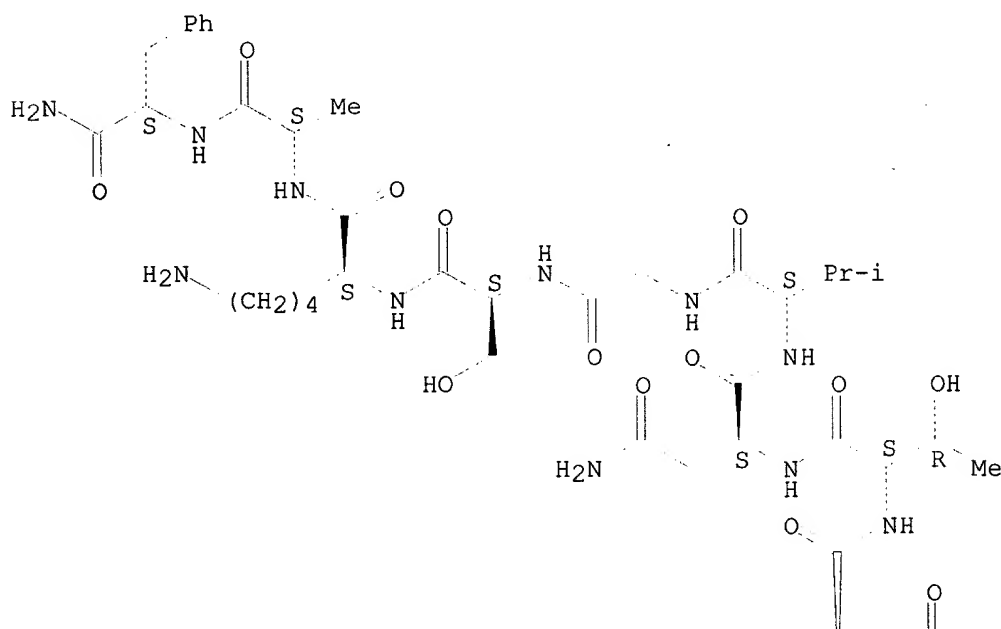
PAGE 2-A



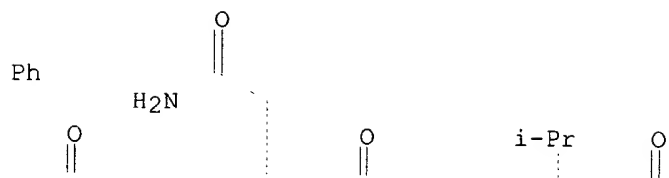
IT 119911-68-1, 8-37-Human CGRP
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); BUU (Biological use, unclassified); BIOL
 (Biological study); USES (Uses)
 (amylin and CGRP antagonist effect on anorectic
 effects of cholecystokinin and bombesin in diabetic and normal rats)
 RN 119911-68-1 CAPLUS
 CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

PAGE 1-A



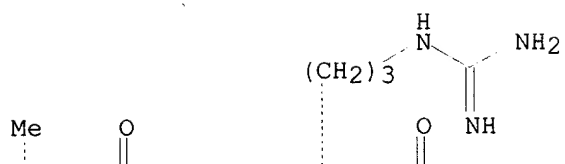
PAGE 1-B



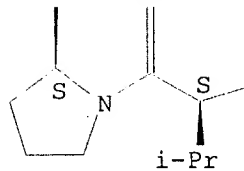
PAGE 1-C



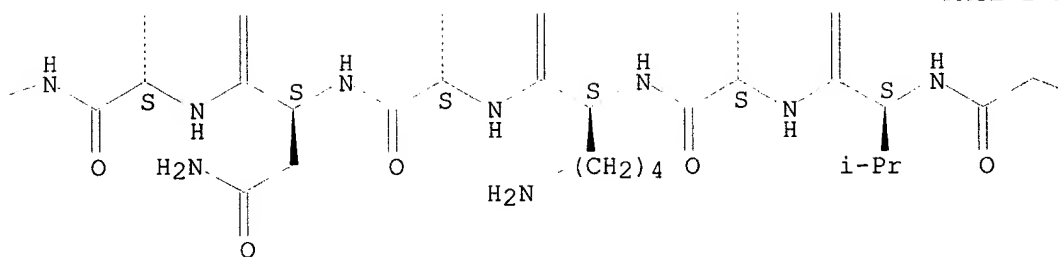
PAGE 1-D

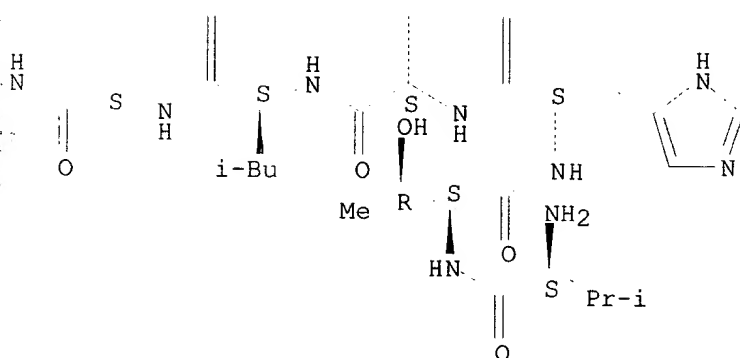
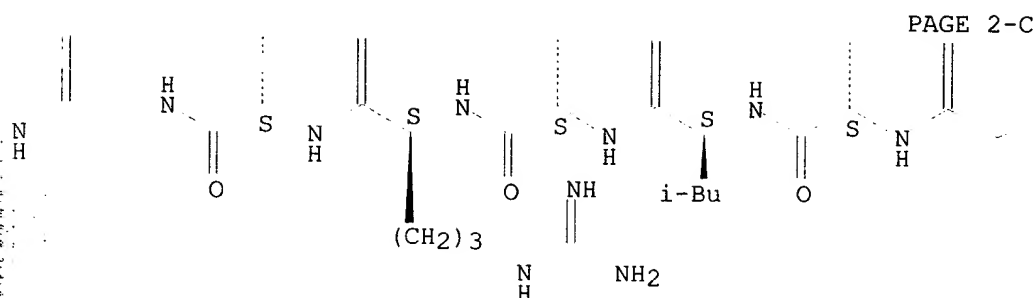


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125 ANSWER 31 OF 48 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:216963 CAPLUS
 DOCUMENT NUMBER: 126:288512
 TITLE: Inhibition by adrenomedullin of the adrenergic neurogenic response in canine mesenteric arteries
 AUTHOR(S): Okamura, Tomio; Zhang, Jian-Xin; Kangawa, Kenji; Toda, Noboru
 CORPORATE SOURCE: Department of Pharmacology, Shiga University of Medical Science, Seta, 520-21, Japan
 SOURCE: Japanese Journal of Pharmacology (1997), 73(3), 259-261
 CODEN: JJPAAZ; ISSN: 0021-5198
 PUBLISHER: Japanese Pharmacological Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Adrenomedullin (AM) inhibited the pressor action caused by transmural elec. stimulation in perfused isolated canine mesenteric arteries. The inhibitory potency of AM was greater than that of calcitonin gene-related peptide (CGRP) or proadrenomedullin NH2-terminal 20 peptide. [8 -37]CGRP did not affect the inhibitory action of AM, but suppressed the CGRP-induced inhibition. It may be concluded that AM has an ability to inhibit adrenergic neuronal transmission without the mediation of CGRP1 receptors in the peripheral vasculature, and this inhibition partly participates in the potent hypotensive action of AM.

IT 150238-87-2, Human PAMP 20

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

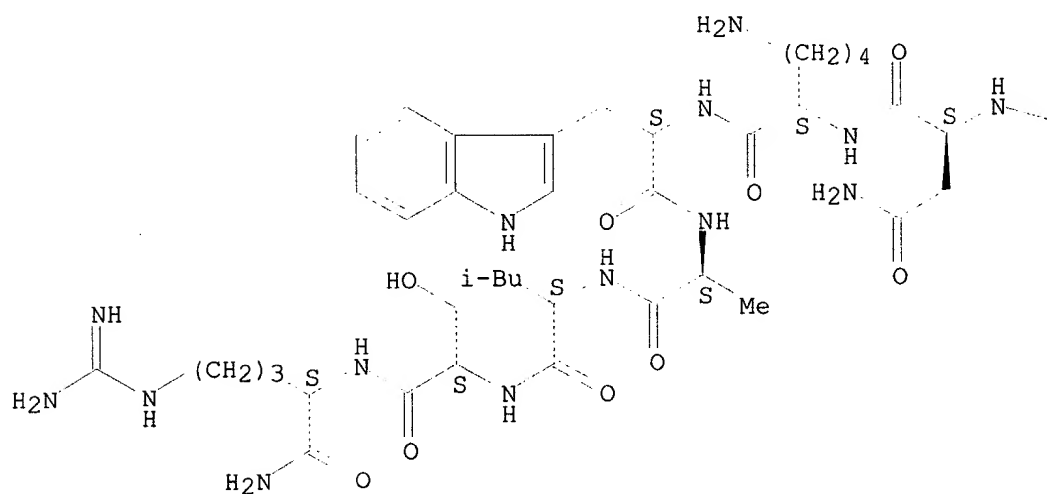
(adrenomedullin inhibition of adrenergic neurogenic response in canine mesenteric arteries)

RN 150238-87-2 CAPLUS

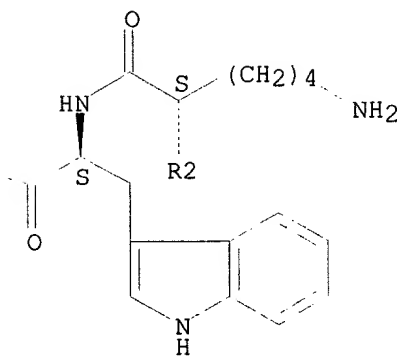
CN L-Argininamide, L-alanyl-L-arginyl-L-leucyl-L-.alpha.-aspartyl-L-valyl-L-alanyl-L-seryl-L-.alpha.-glutamyl-L-phenylalanyl-L-arginyl-L-lysyl-L-lysyl-L-tryptophyl-L-asparaginyl-L-lysyl-L-tryptophyl-L-alanyl-L-leucyl-L-seryl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

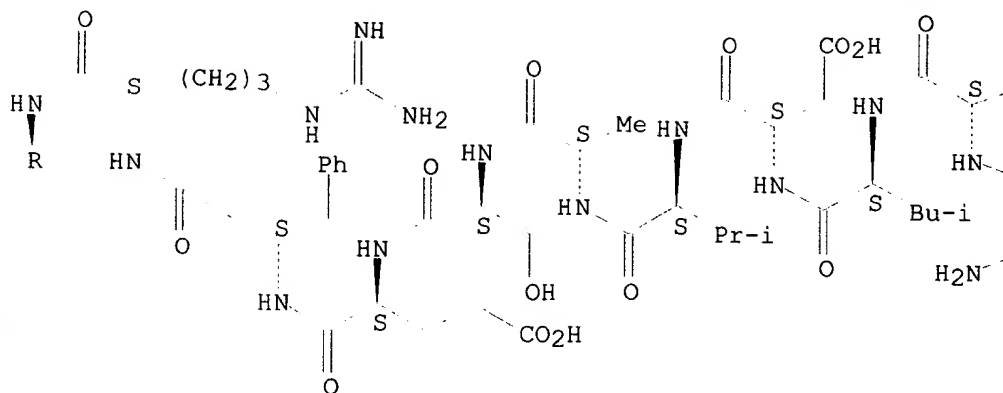
PAGE 1-A



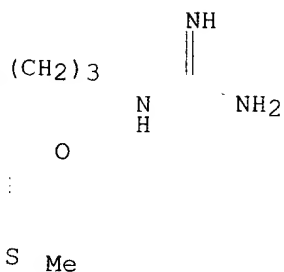
PAGE 1-B



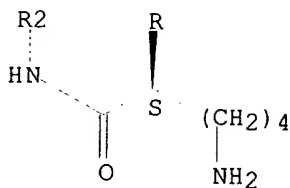
PAGE 2-A



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PAGE 3-A



L25 ANSWER 32 OF 48 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:156262 CAPLUS
 DOCUMENT NUMBER: 126:181666
 TITLE: **Inhibitory effects of calcitonin gene-related peptide on substance-P-induced superoxide production in human neutrophils.** [Erratum to document cited in CA126:1505]
 AUTHOR(S): Tanabe, Takatoshi; Otani, Hitomi; Zeng, Xun-Ting; Mishima, Katsuyuki; Ogawa, Ryoukei; Inagaki, Chiyoko
 CORPORATE SOURCE: Dep. Pharmacol., Kansai Med. Univ., Osaka, 570, Japan
 SOURCE: European Journal of Pharmacology (1997), 321(1), 137-141
 CODEN: EJPHAZ; ISSN: 0014-2999
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Figs. 1-6 are reprinted. The errors were not reflected in the abstr. or the index entries.

IT 33507-63-0, Substance P (peptide)

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

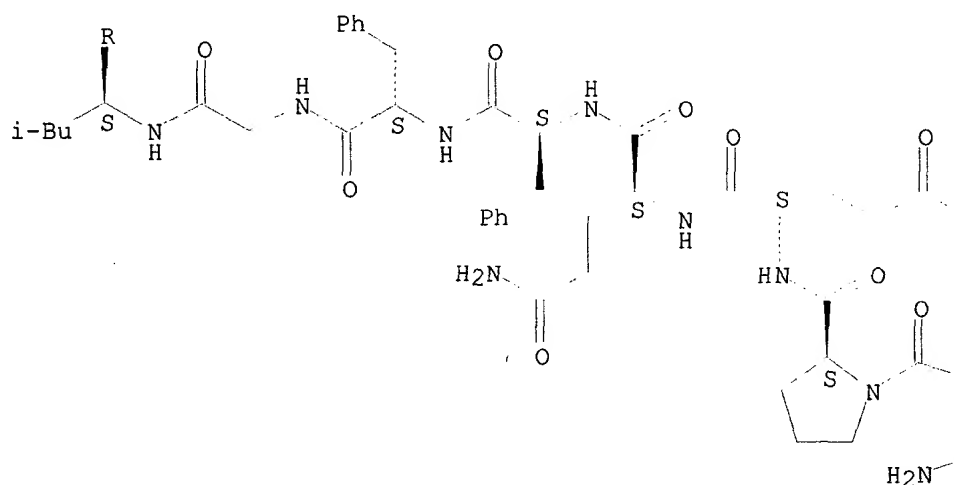
(CGRP inhibitory effects on substance-P-induced superoxide prodn. in human neutrophils and mechanism therefor (Erratum))

RN 33507-63-0 CAPLUS

CN Substance P (9CI) (CA INDEX NAME)

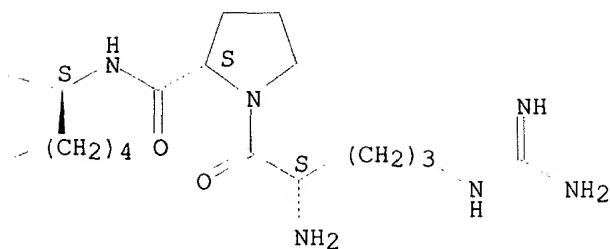
Absolute stereochemistry.

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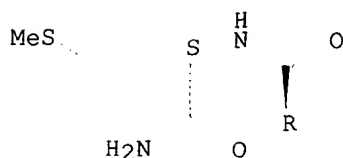


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NH₂



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L25 ANSWER 33 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:121756 CAPLUS

DOCUMENT NUMBER: 126:195706

TITLE: Adrenomedullin-(22-52) **antagonizes**
vasodilator responses to **CGRP** but not
adrenomedullin in the catAUTHOR(S): Champion, Hunter C.; Santiago, Jose A.; Murphy,
William A.; Coy, David H.; Kadowitz, Philip J.CORPORATE SOURCE: Dep. Pharmacology Med., Tulane Univ. Sch. Med., New
Orleans, LA, 70112, USASOURCE: American Journal of Physiology (1997), 272(1, Pt. 2),
R234-R242

CODEN: AJPHAP; ISSN: 0002-9513

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of adrenomedullin (ADM)-(22-52), a putative ADM receptor antagonist, on vasodilator responses to ADM and the structurally related peptide, calcitonin gene-related peptide (CGRP), were investigated in the hindlimb vascular bed of the cat under const.-flow conditions. ADM-(22-52) had no significant effect on hindlimb perfusion pressure when injected in doses up to 120 nmol; after administration of ADM-(22-52), vasodilator responses to ADM were unchanged, whereas vasodilator responses to CGRP were inhibited. The inhibitory effects of ADM-(22-52) on responses to CGRP were selective and reversible and were similar to the inhibitory effects of the CGRP antagonist CGRP-(8-37). Hindlimb vasodilator responses to CGRP and to ADM were increased in duration by the cAMP phosphodiesterase inhibitor rolipram but were not altered by inhibitors of cGMP phosphodiesterase, nitric oxide synthetase, K⁺-ATP channels, the cyclooxygenase pathway, or the adrenergic nervous system. These results demonstrate that ADM-(22-52) is a selective CGRP receptor antagonist in the hindlimb vascular bed of the cat. The present data suggest that vasodilator responses to CGRP and ADM are mediated by different receptors but that these peptides dilate the hindlimb vascular bed of the cat by a similar cAMP-dependent mechanism.

IT 119911-68-1, Human **CGRP**-(8-37) 129121-73-9,Rat **CGRP**-(8-37) 159899-65-7, Human

Adrenomedullin-(22-52)

RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); BIOL (Biological study)

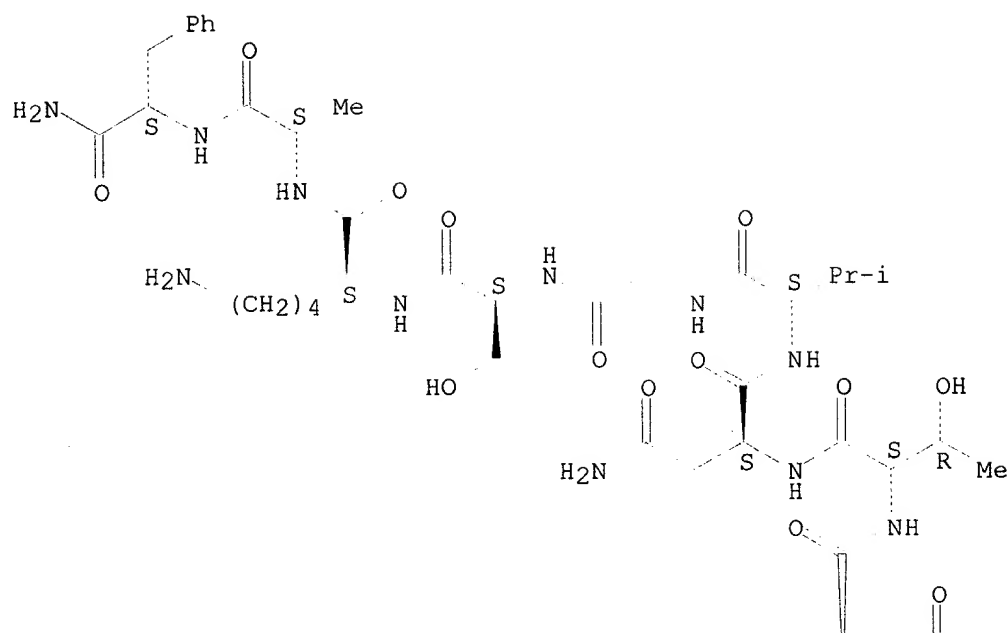
(adrenomedullin-(22-52) **antagonizes** vasodilator responses to
CGRP but not adrenomedullin in cat)

RN 119911-68-1 CAPLUS

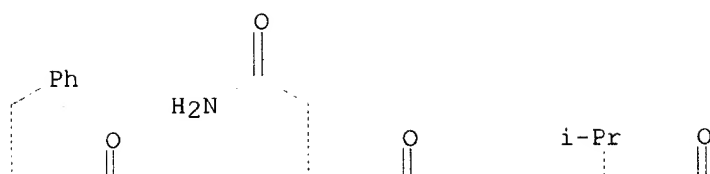
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

PAGE 1-A



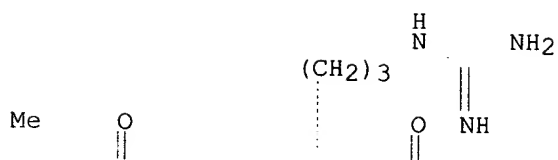
PAGE 1-B



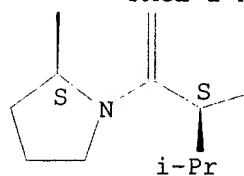
PAGE 1-C



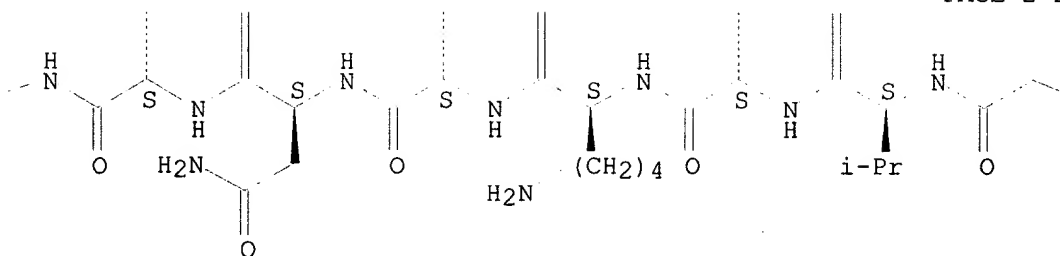
PAGE 1-D



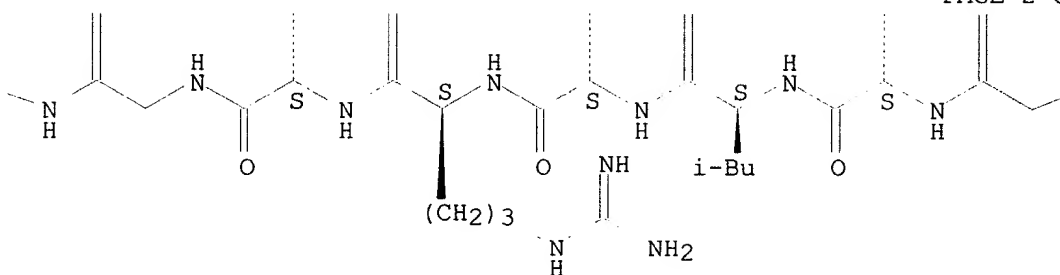
PAGE 2-A



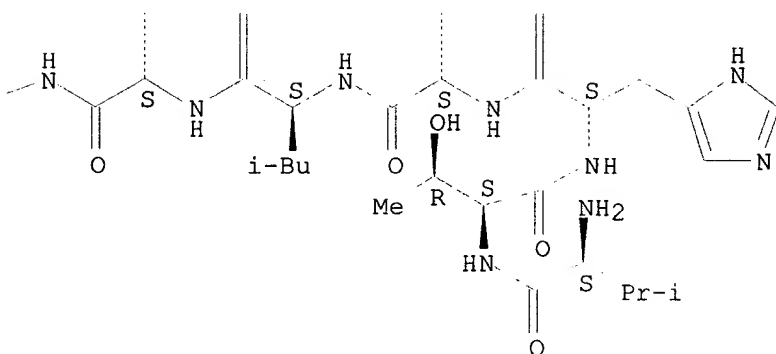
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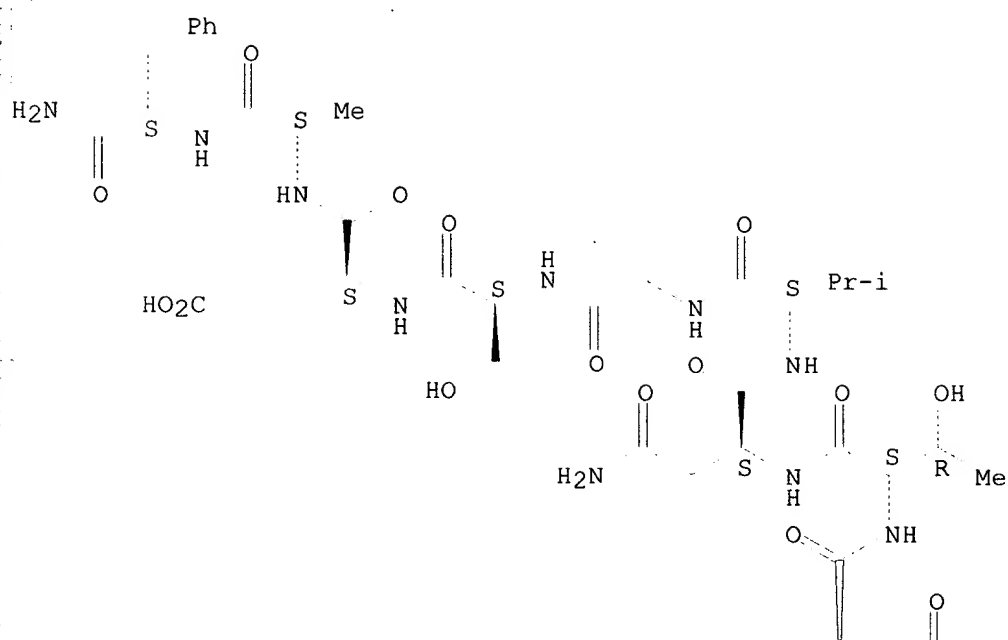
PAGE 2-D



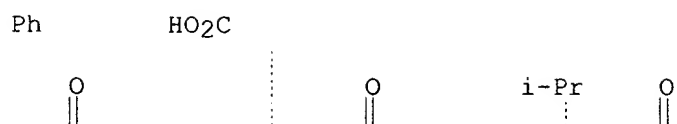
RN 129121-73-9 CAPLUS
CN 8-37-.alpha.-Calcitonin gene-related peptide (rat reduced) (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



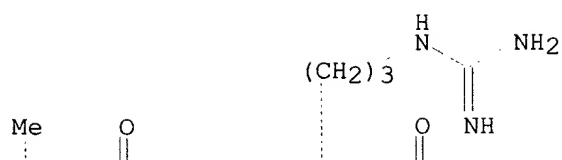
PAGE 1-B



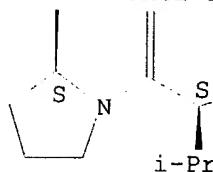
PAGE 1-C



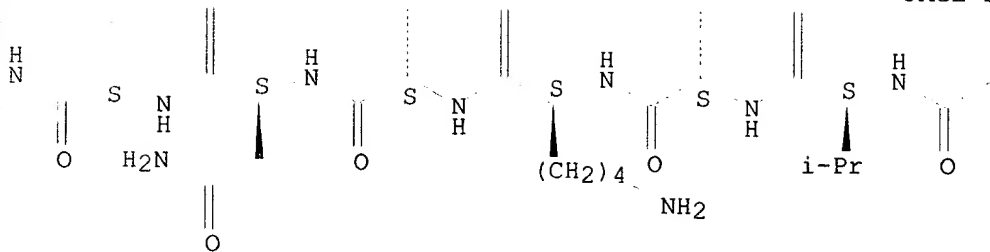
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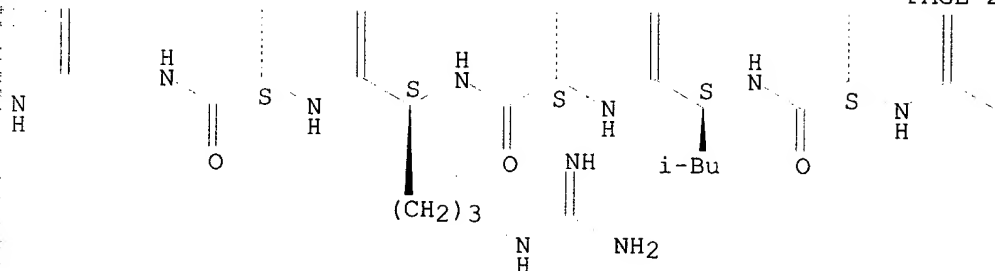
PAGE 2-A



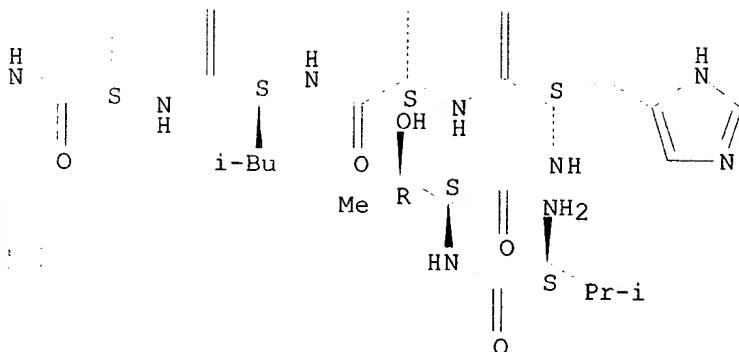
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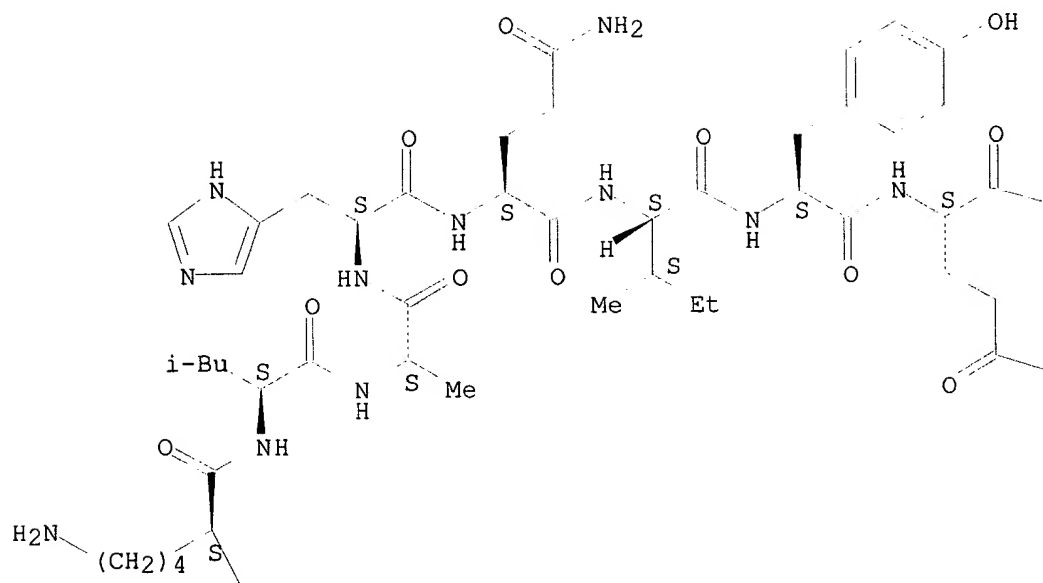


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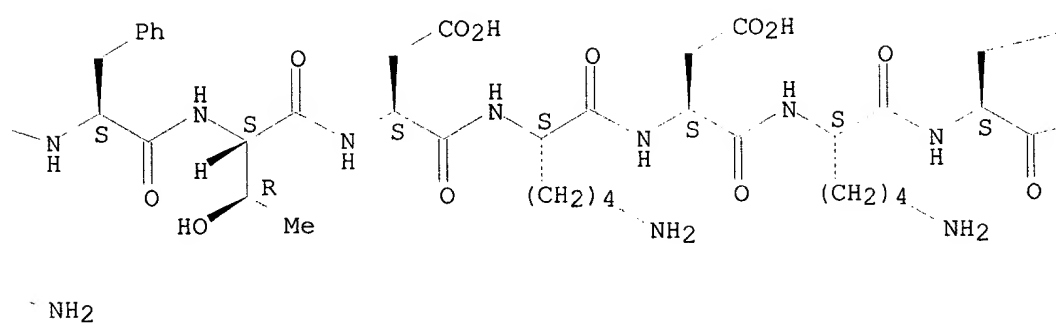


RN 159899-65-7 CAPLUS
 CN L-Tyrosinamide, L-threonyl-L-valyl-L-glutaminyl-L-lysyl-L-leucyl-L-alanyl-L-histidyl-L-glutaminyl-L-isoleucyl-L-tyrosyl-L-glutaminyl-L-phenylalanyl-L-threonyl-L-.alpha.-aspartyl-L-lysyl-L-.alpha.-aspartyl-L-lysyl-L-.alpha.-aspartyl-L-asparaginyl-L-valyl-L-alanyl-L-prolyl-L-arginyl-L-seryl-L-lysyl-L-isoleucyl-L-seryl-L-prolyl-L-glutaminylglycyl- (9CI) (CA INDEX NAME)

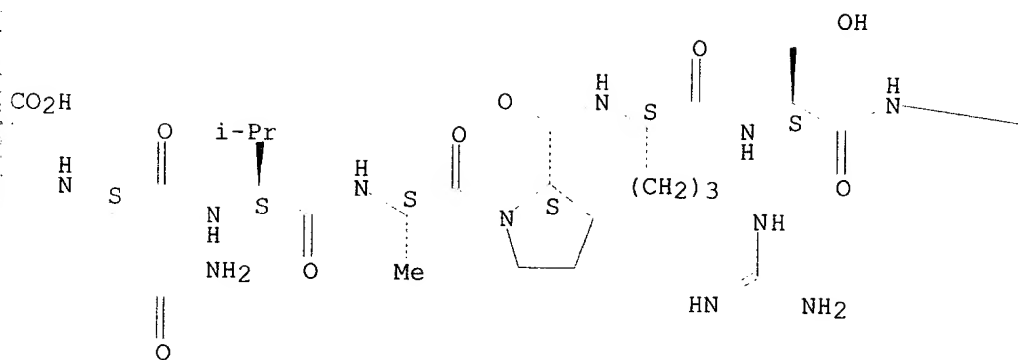
PAGE 1-A



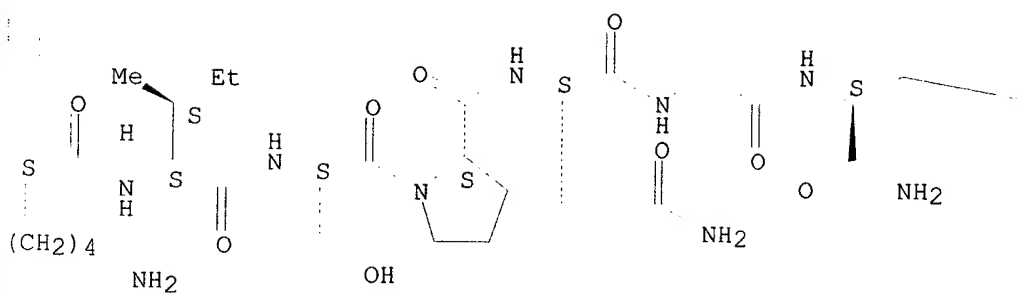
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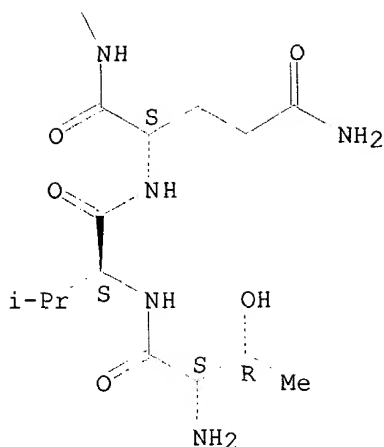
PAGE 1-D



PAGE 1-E

OH

PAGE 2-A



L25 ANSWER 34 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:756512 CAPLUS

DOCUMENT NUMBER: 126:1505

TITLE: **Inhibitory effects of calcitonin****gene-related peptide on**

substance-P-induced superoxide production in human neutrophils

AUTHOR(S):

Tanabe, Takatoshi; Otani, Hitomi; Zeng, Xun-Ting; Mishima, Katsuyuki; Ogawa, Ryoukei; Inagaki, Chiyoko
Dep. Pharmacol., Kansai Med. Univ., Osaka, 570, Japan
European Journal of Pharmacology (1996), 314(1/2), 175-183

CORPORATE SOURCE:

SOURCE:

CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER:

Elsevier

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB We examd. the mechanisms of the inhibitory effects of calcitonin gene-related peptide (CGRP) on substance-P-induced superoxide anion (O₂⁻) prodn. in human neutrophils. Substance P (30 .mu.M) caused O₂⁻ prodn. assocd. with an inositol-1,4,5-trisphosphate (IP₃)-induced transient increase in intracellular Ca²⁺ concns. ([Ca²⁺]_i). CGRP (10 .mu.M) significantly inhibited substance-P-induced O₂⁻ prodn. and transient increase in [Ca²⁺]_i, but it only slightly suppressed IP₃ formation. In addn., CGRP inhibited IP₃-induced O₂⁻ prodn. and transient increase in [Ca²⁺]_i caused by exogenous addn. of IP₃ in saponin-permeabilized neutrophils. These findings suggest that CGRP inhibits the response of neutrophils to substance P through the inhibition of IP₃-induced Ca²⁺ release from intracellular Ca²⁺ stores. The inhibitory effects of CGRP on substance P- or IP₃-induced O₂⁻ prodn. and increases in [Ca²⁺]_i were abolished by pretreating the neutrophils with a CGRP receptor antagonist, CGRP-(8-37), or cAMP-dependent protein kinase inhibitors, H-8 and KT 5720. We concluded that CGRP receptor stimulation reduces substance-P-induced O₂⁻ prodn. by the inhibition of IP₃-induced transient increase in [Ca²⁺]_i, probably via the phosphorylation of IP₃ receptor by cAMP-dependent protein kinase.

IT 33507-63-0, Substance P (peptide)

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); BIOL (Biological study)

(CGRP inhibitory effects on substance-P-induced

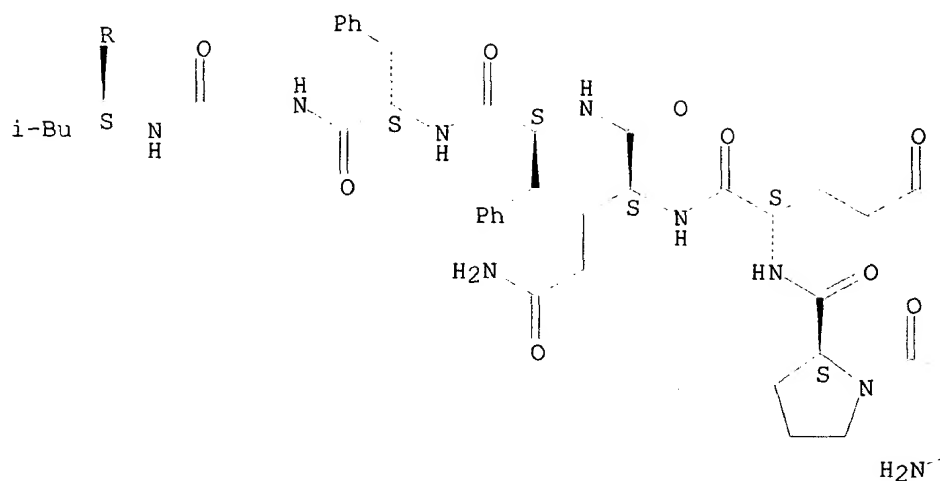
superoxide prodn. in human neutrophils and mechanism therefor)

RN 33507-63-0 CAPLUS

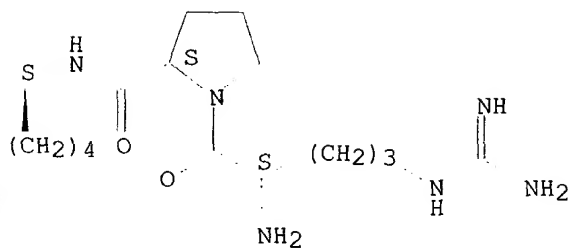
CN Substance P (9CI) (CA INDEX NAME)

Absolute stereochemistry.

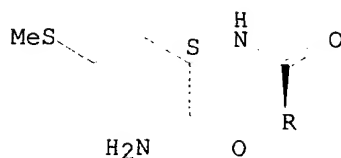
PAGE 1-A



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NH₂

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DOCUMENT NUMBER: 126:26933
TITLE: Design of receptor selective peptides that antagonize the actions of amylin in vivo
AUTHOR(S): Prickett, K. S.; Albrecht, E.; Soares, C. J.; Lumpkin, R. H.; Gaeta, L. S. L.; Moore, C. X.; Young, A. A.; Beeley, N. R. A.; Beaumont, K.
CORPORATE SOURCE: Amylin Pharmaceuticals, Inc., San Diego, CA, 92121, USA
SOURCE: Peptides: Chemistry, Structure and Biology, Proceedings of the American Peptide Symposium, 14th, Columbus, Ohio, June 18-23, 1995 (1996), Meeting Date 1995, 620-622. Editor(s): Kaumaya, Pravin T. P.; Hodges, Robert S. Mayflower Scientific: Kingswinford, UK.
CODEN: 63NTAF
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The authors have identified two series of peptides, which inhibit binding of amylin to its receptor in nucleus accumbens membranes and are effective in vivo in antagonizing metabolic actions of amylin. Two of these peptides AC253 (Ac-LGRLSQELHRLQTYPRNTGSENTY-NH₂) and AC625 (Ac-ATQRLANELVRLQTYPRTNVGSNTY-NH₂) have been further evaluated preclinically and in Phase I clin. studies.

IT **119911-68-1**, 8-37-.alpha.-Calcitonin gene-related peptide (human reduced) **138398-61-5**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

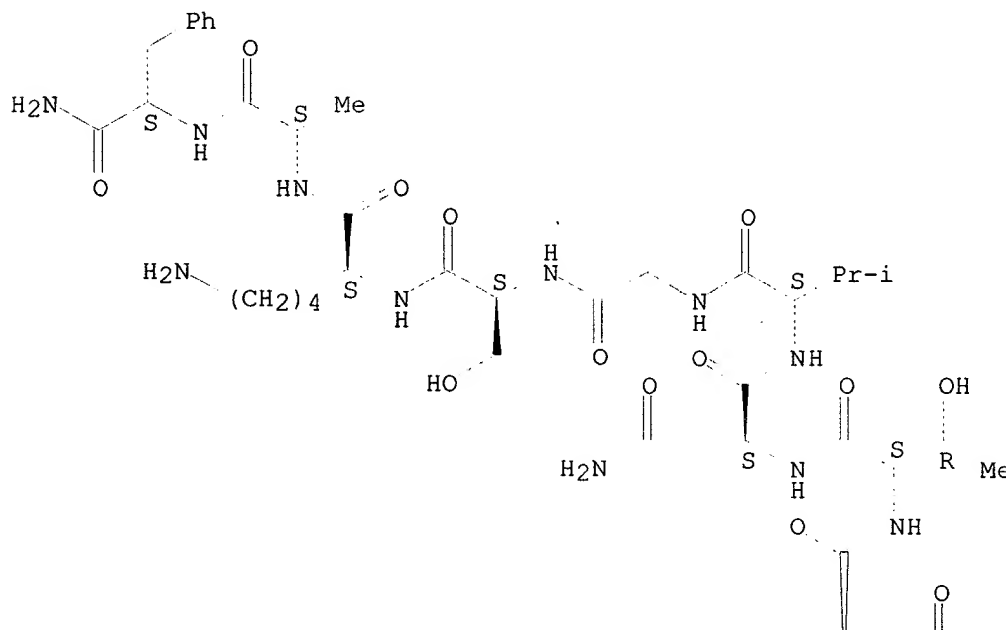
(design of **receptor** selective peptides that **antagonize** actions of amylin in vivo)

RN 119911-68-1 CAPLUS

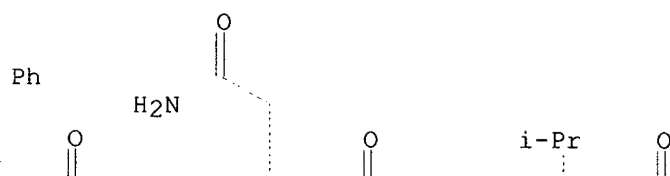
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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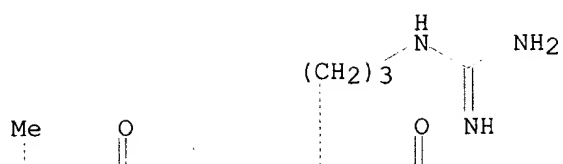
PAGE 1-B



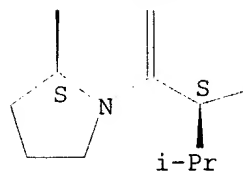
PAGE 1-C



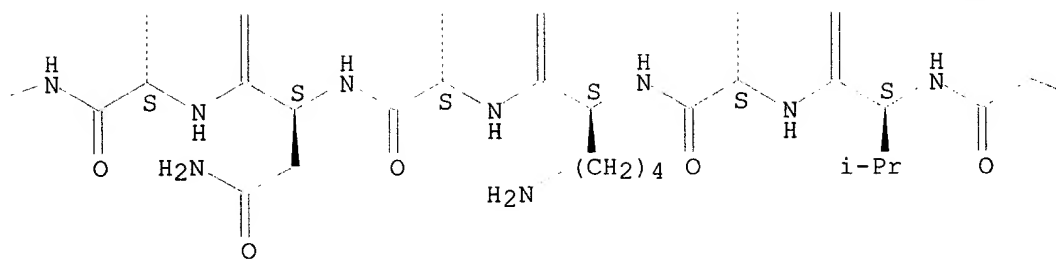
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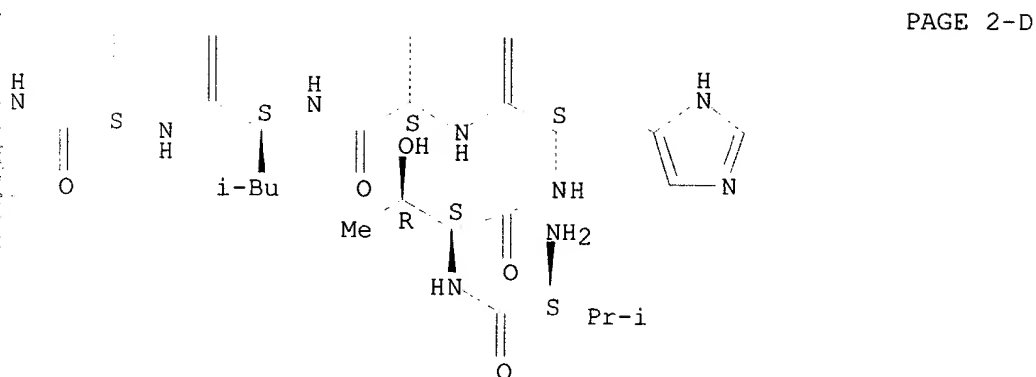
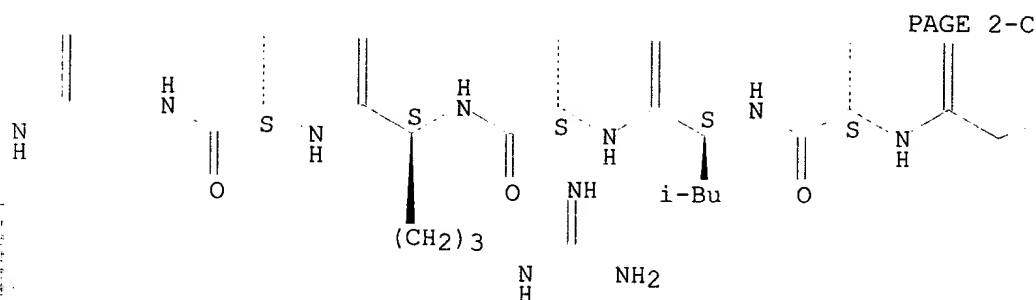


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PAGE 2-B

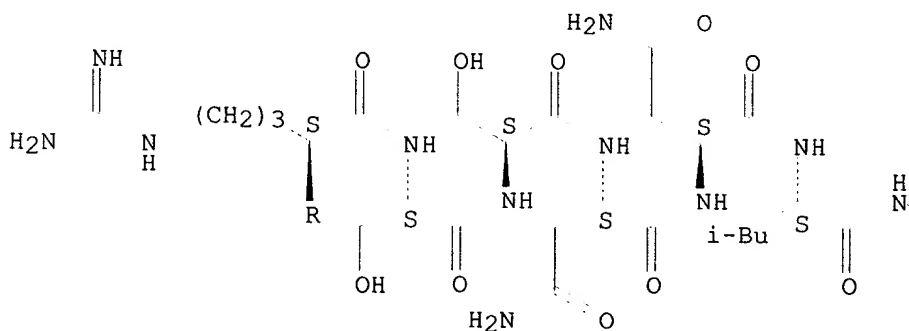




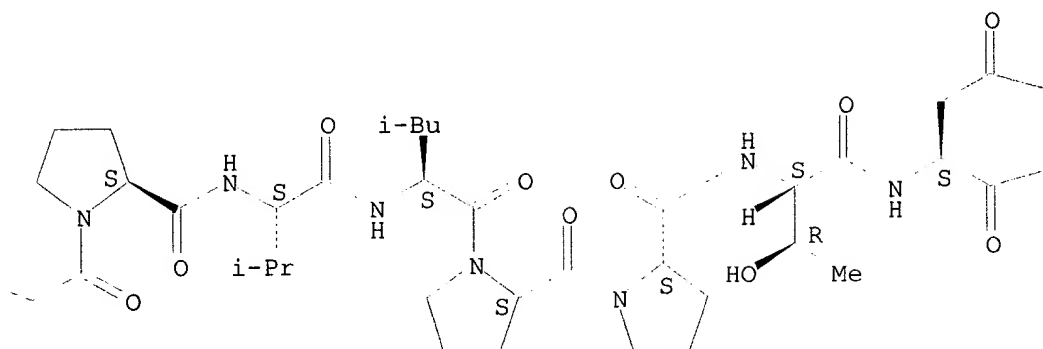
RN 138398-61-5 CAPLUS
 CN L-Tyrosinamide, L-alanyl-L-threonyl-L-glutamyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-arginyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-leucylglycyl-L-prolyl-L-valyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

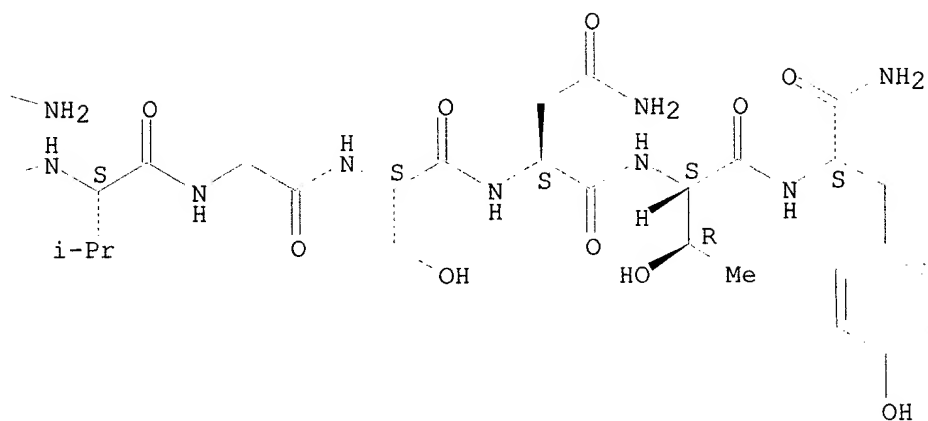
PAGE 1-A



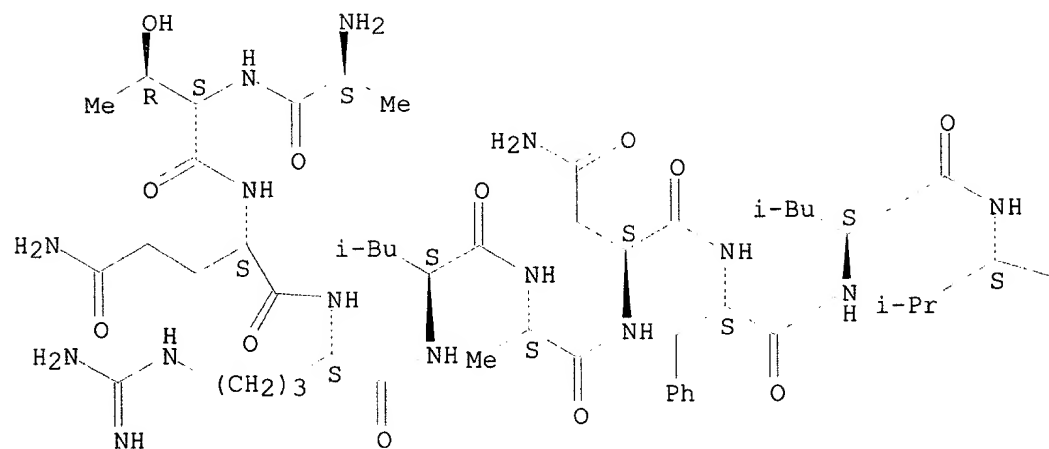
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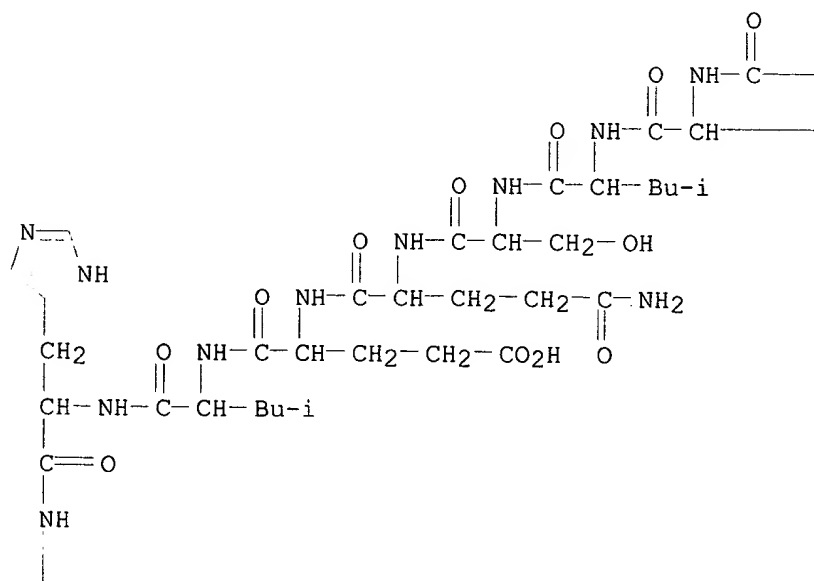
PAGE 2-B

R
|
NH

||
O

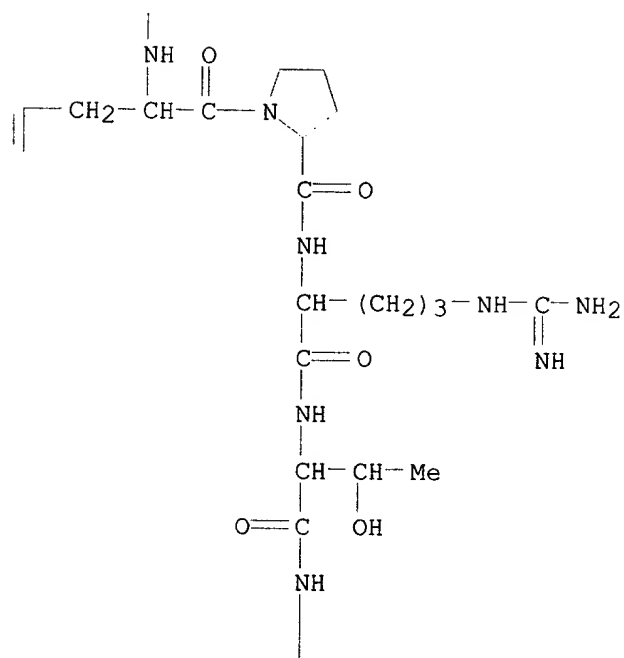
IT 144500-19-6P 151804-77-2P 151804-79-4P
151804-85-2P 155069-90-2P, 8-32-Calcitonin (salmon
reduced) 163860-07-9P 163860-08-0P
163860-09-1P 163894-44-8P 184581-35-9P
184581-36-0P 184581-37-1P 184581-38-2P
184581-39-3P 184581-40-6P 184581-41-7P
184581-42-8P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); PRP (Properties); SPN (Synthetic
preparation); BIOL (Biological study); PREP (Preparation)
(design of receptor selective peptides that antagonize actions of
amylin in vivo)
RN 144500-19-6 CAPLUS
CN Calcitonin (salmon reduced), 1-de-L-cysteine-2-de-L-serine-3-de-L-
asparagine-4-de-L-leucine-5-de-L-serine-6-de-L-threonine-7-de-L-cysteine-8-
(N-acetyl-L-valine)- (9CI) (CA INDEX NAME)

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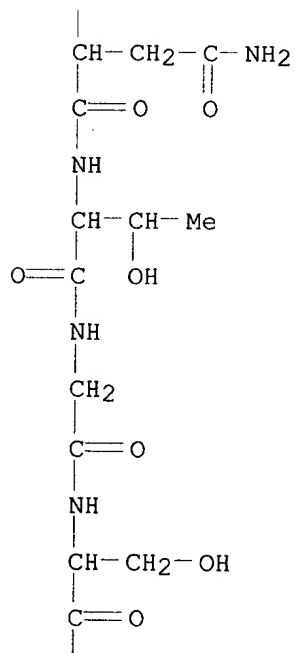


$$\begin{array}{c} \text{O} \quad \text{NHAc} \\ \parallel \quad | \\ \text{NH}-\text{C}-\text{CH}-\text{Pr-i} \\ | \quad | \\ \text{O} \quad \text{NH} \\ \parallel \quad | \\ \text{CH}_2-\text{NH}-\text{C}-\text{CH}-\text{Bu-i} \\ | \\ \text{-(CH}_2)_4\text{-NH}_2 \end{array}$$
$$\begin{array}{c}
 | \\
 \text{CH} - (\text{CH}_2)_4 - \text{NH}_2 \\
 | \\
 \text{C} = \text{O} \\
 | \\
 \text{NH} \\
 | \\
 \text{CH} - \text{Bu-i} \\
 | \\
 \text{C} = \text{O} \\
 | \\
 \text{NH} \\
 | \\
 \text{CH} - \text{CH}_2 - \text{CH}_2 - \overset{\text{O}}{\parallel} \text{C} - \text{NH}_2 \\
 | \\
 \text{C} = \text{O} \\
 | \\
 \text{NH} \quad \text{OH} \\
 | \quad | \\
 \text{CH} - \text{CH} - \text{Me} \\
 | \\
 \text{C} = \text{O}
 \end{array}$$

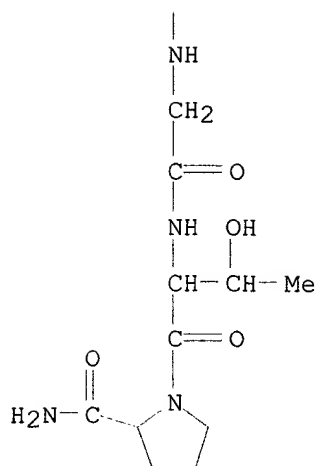
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PAGE 5-A

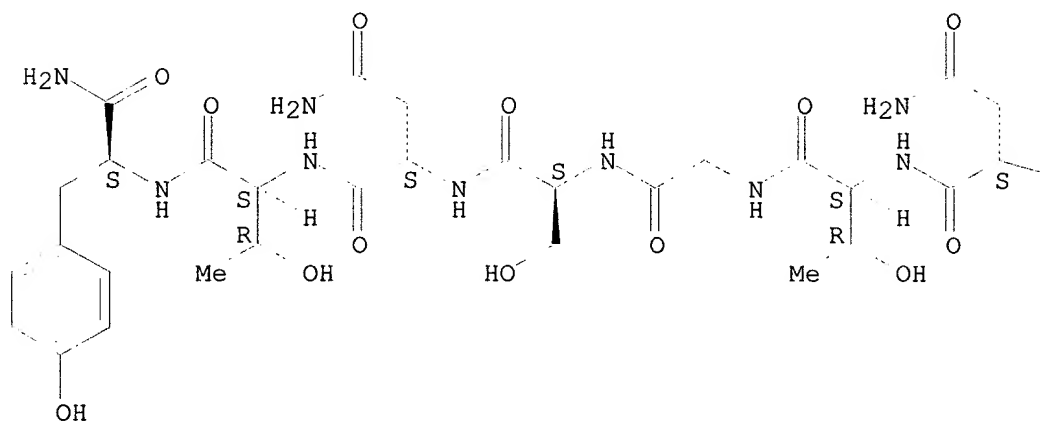


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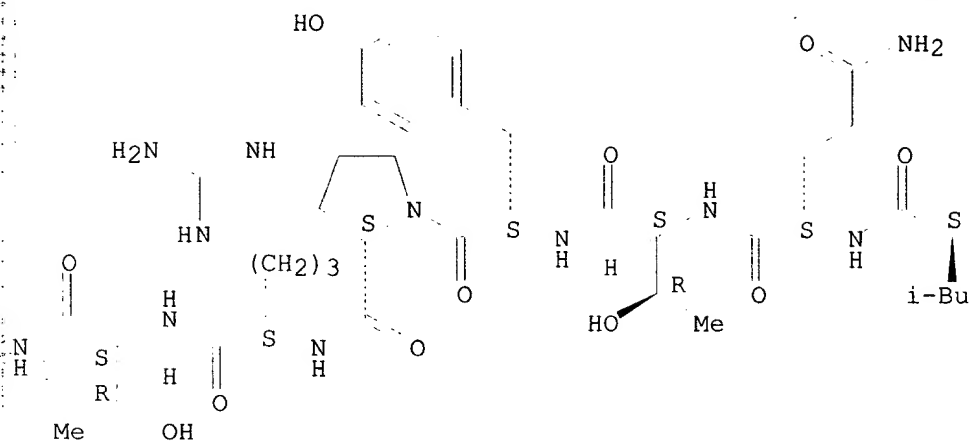
CN 8-32-Calcitonin (salmon reduced), N-acetyl-30-L-asparagine-32-L-tyrosinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

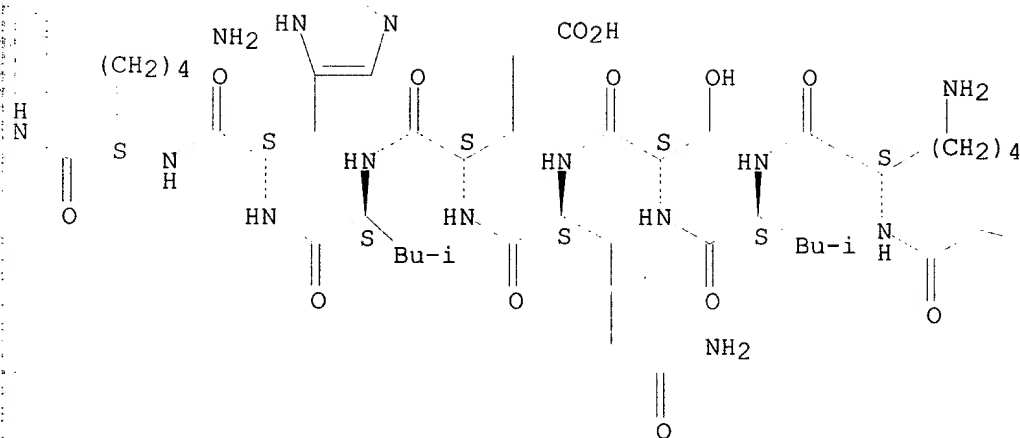
PAGE 1-A



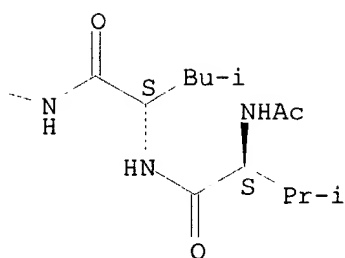
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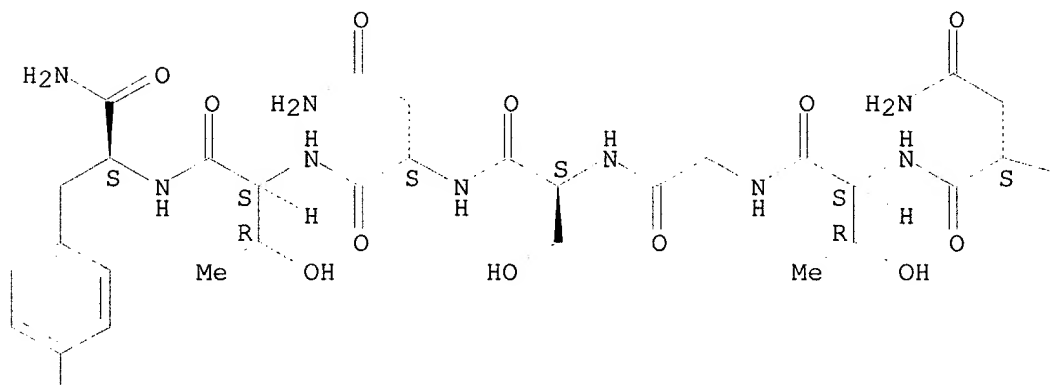
PAGE 1-D



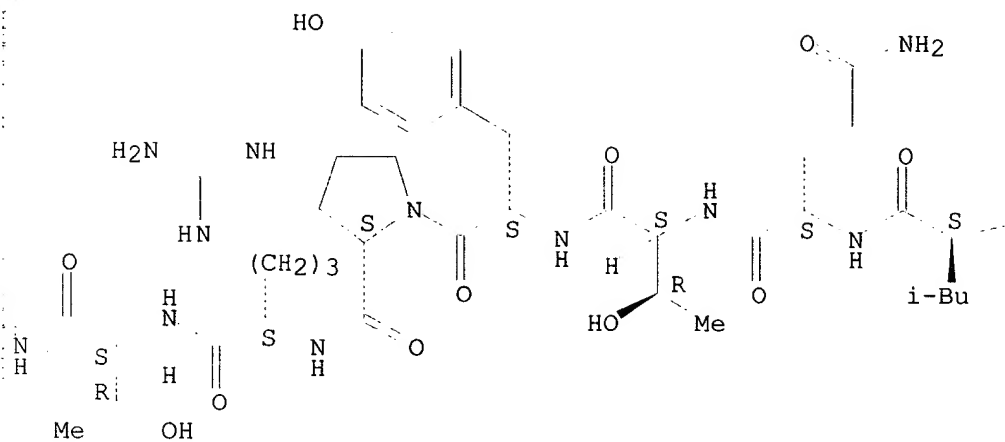
RN 151804-79-4 CAPLUS
CN L-Tyrosinamide, N-acetyl-L-leucylglycyl-L-arginyl-L-leucyl-L-seryl-L-glutamyl-L-.alpha.-glutamyl-L-leucyl-L-histidyl-L-arginyl-L-leucyl-L-glutamyl-L-threonyl-L-tyrosyl-L-prolyl-L-arginyl-L-threonyl-L-asparaginy-L-threonylglycyl-L-seryl-L-asparaginy-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

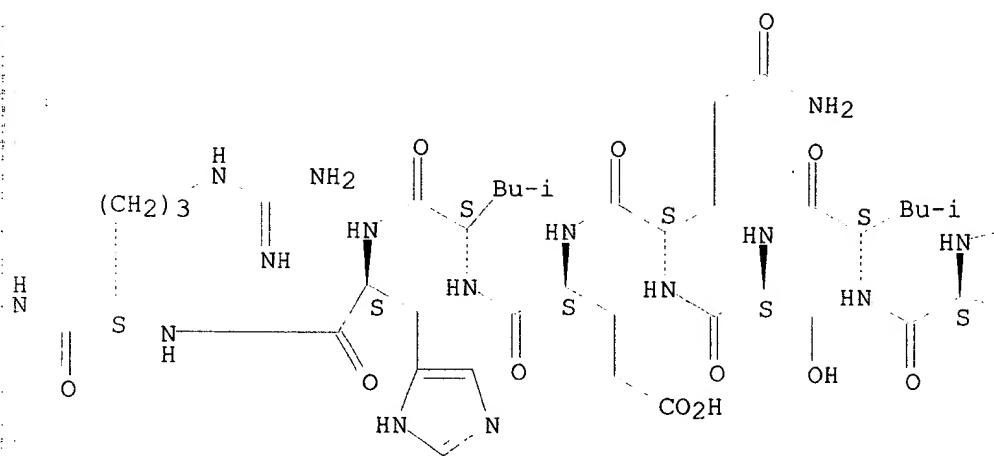
PAGE 1-A



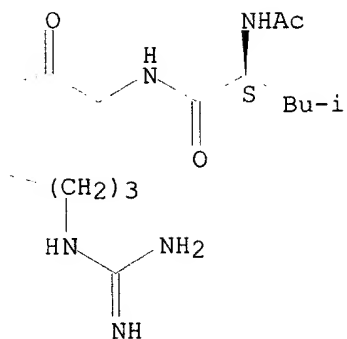
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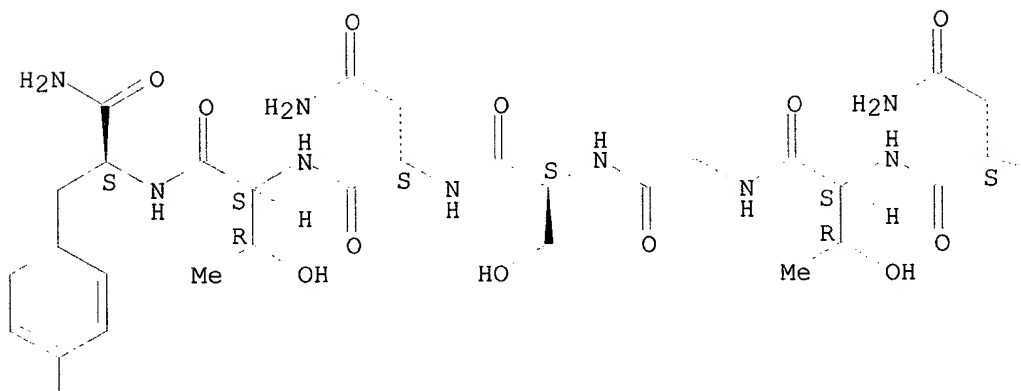
PAGE 2-A



RN 151804-85-2 CAPLUS
 CN Calcitonin (salmon reduced), 1-de-L-cysteine-2-de-L-serine-3-de-L-asparagine-4-de-L-leucine-5-de-L-serine-6-de-L-threonine-7-de-L-cysteine-8-de-L-valine-9-(N-acetyl-L-leucine)-18-L-arginine-30-L-asparagine-32-L-tyrosinamide- (9CI) (CA INDEX NAME)

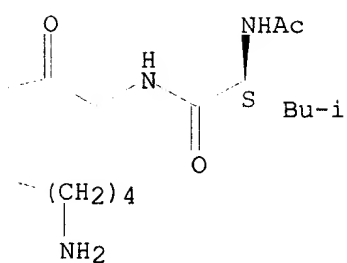
Absolute stereochemistry.

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[illegible]

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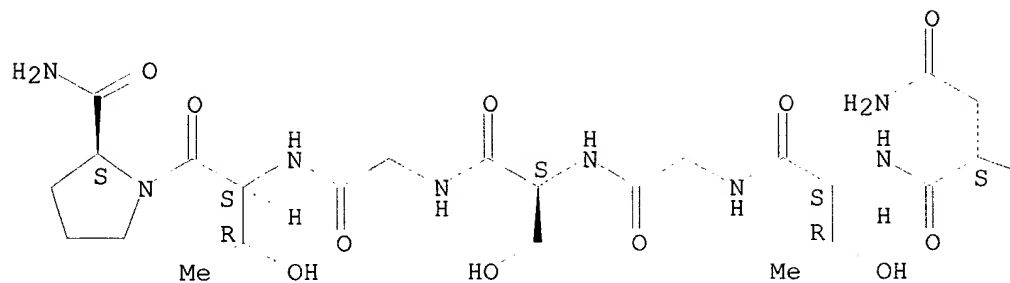
PAGE 2-A



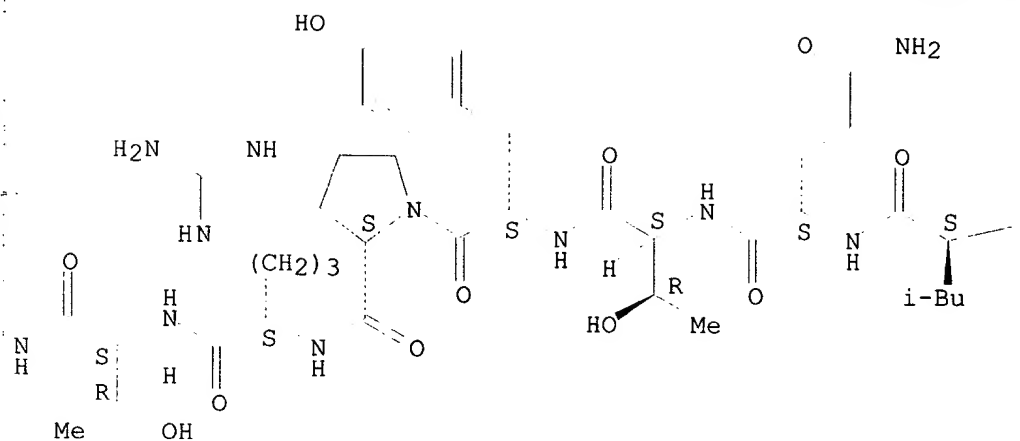
RN 155069-90-2 CAPLUS
CN 8-32-Calcitonin (salmon reduced) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

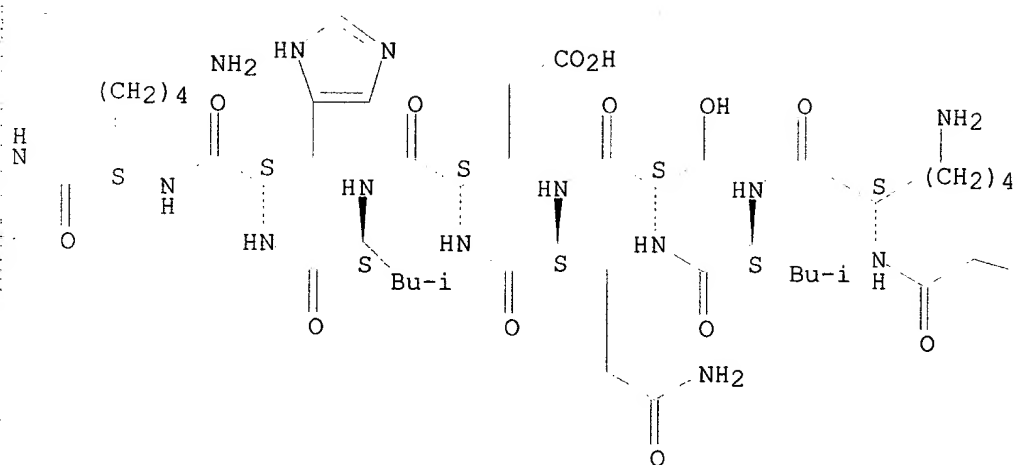
PAGE 1-A



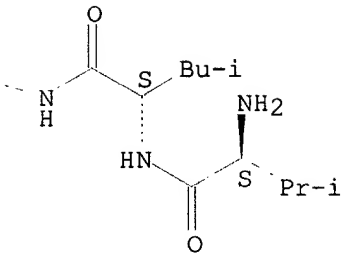
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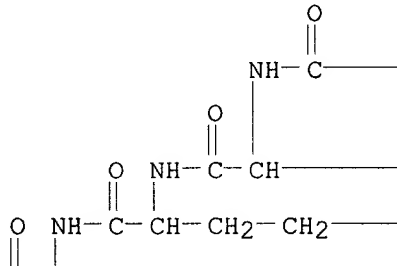


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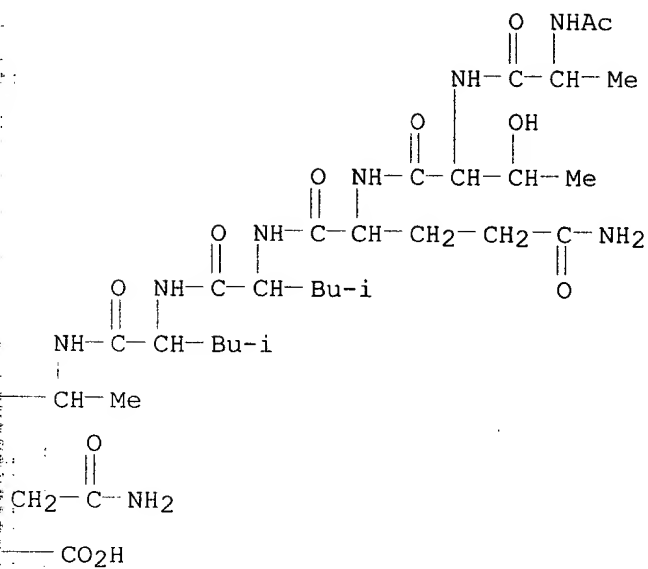


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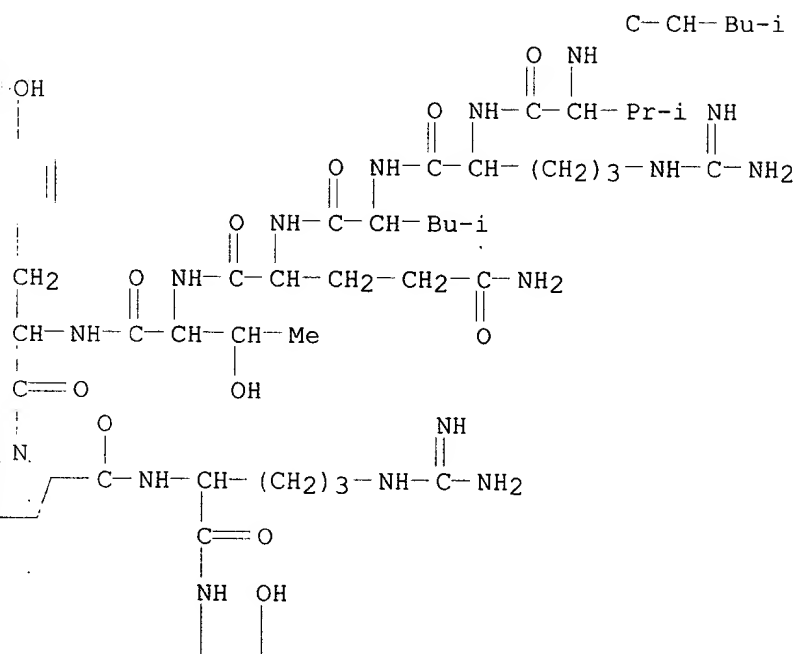
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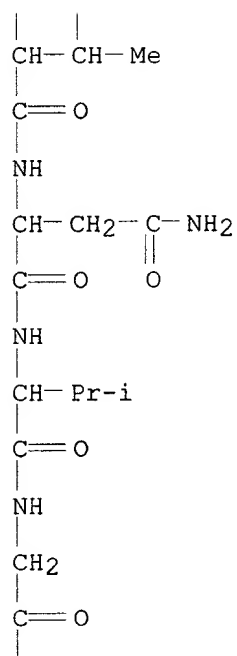
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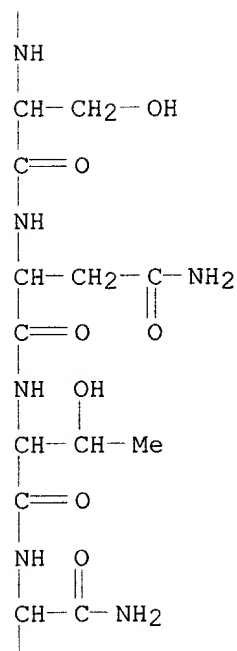
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PAGE 4-A



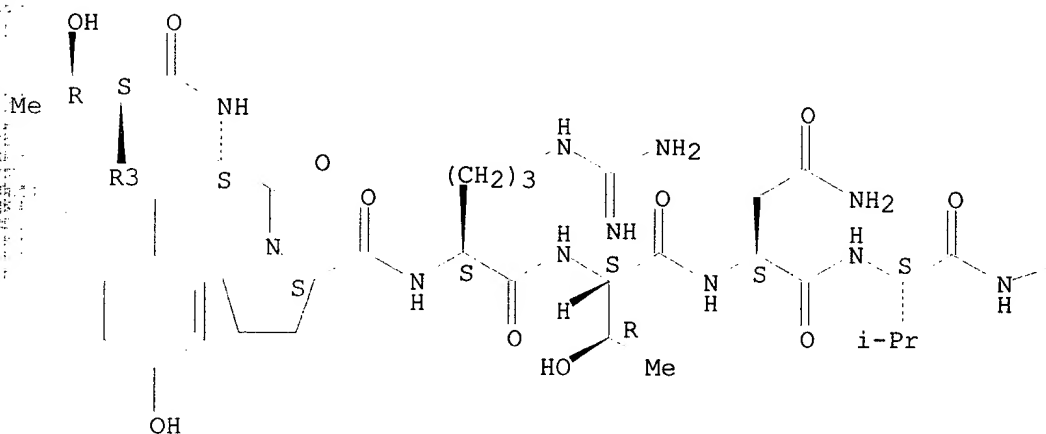
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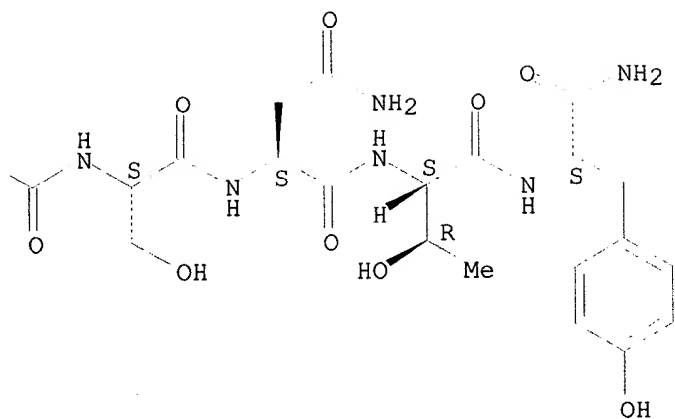
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Absolute stereochemistry.

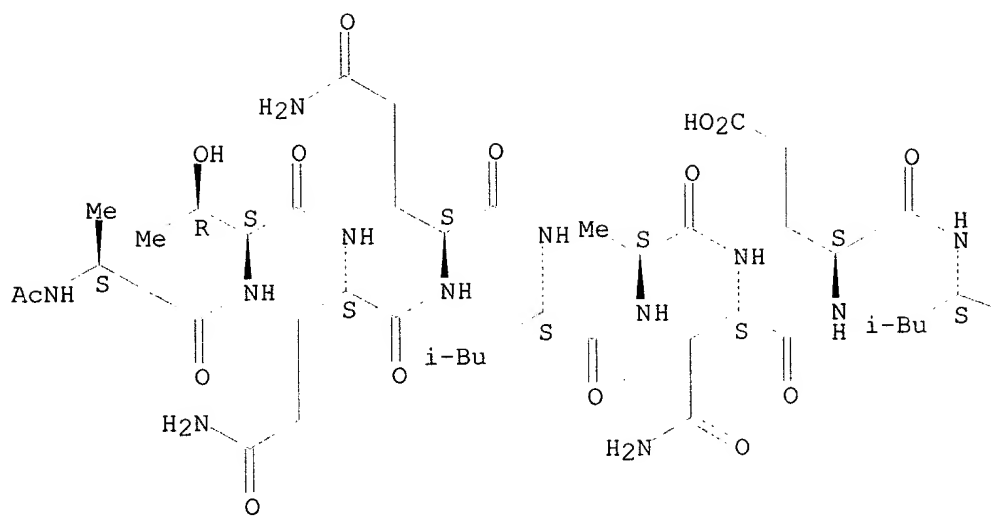
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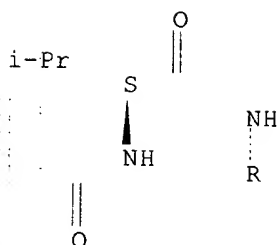
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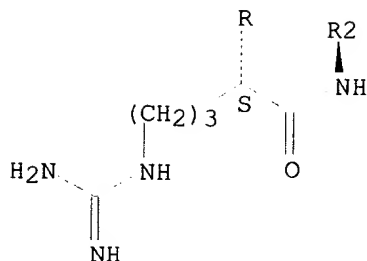
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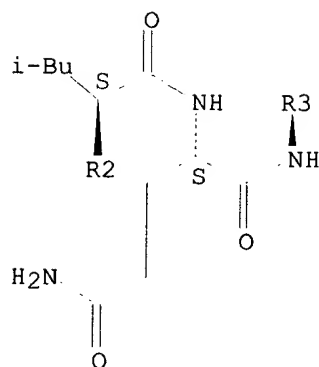
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PAGE 3-A



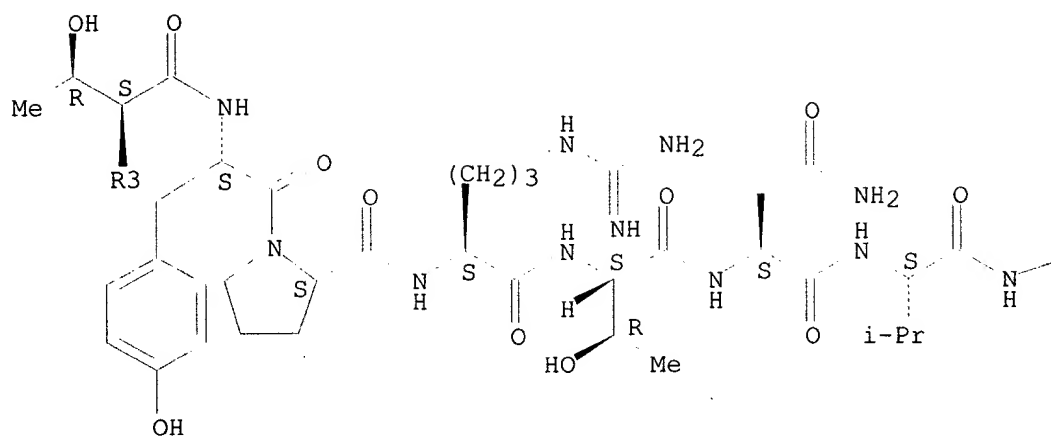
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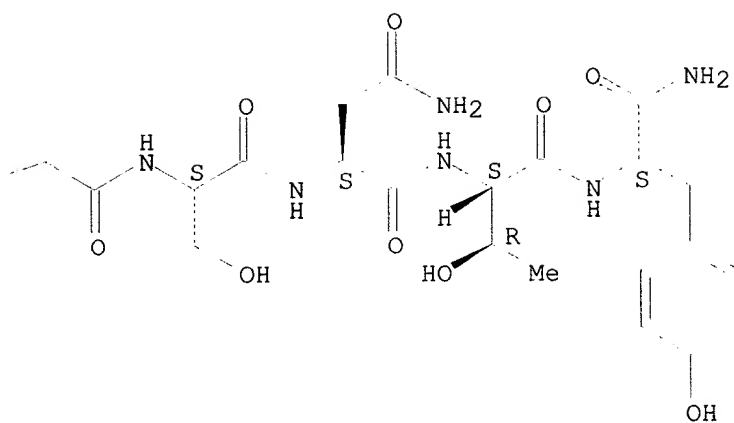
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Absolute stereochemistry.

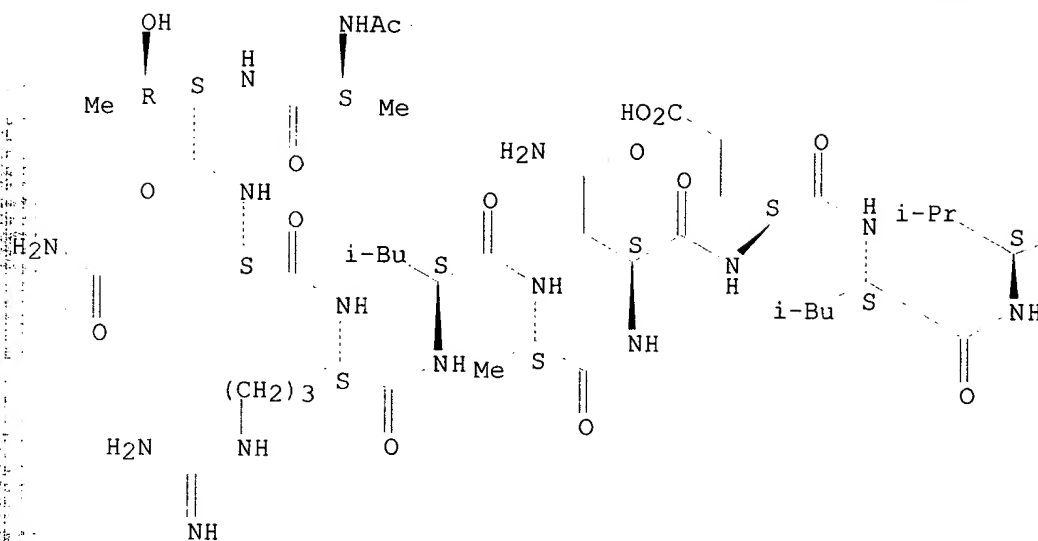
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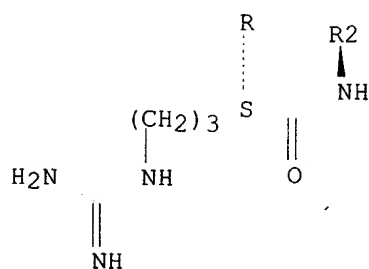
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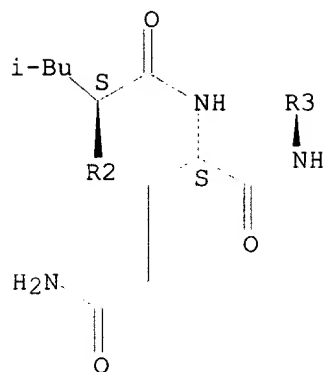
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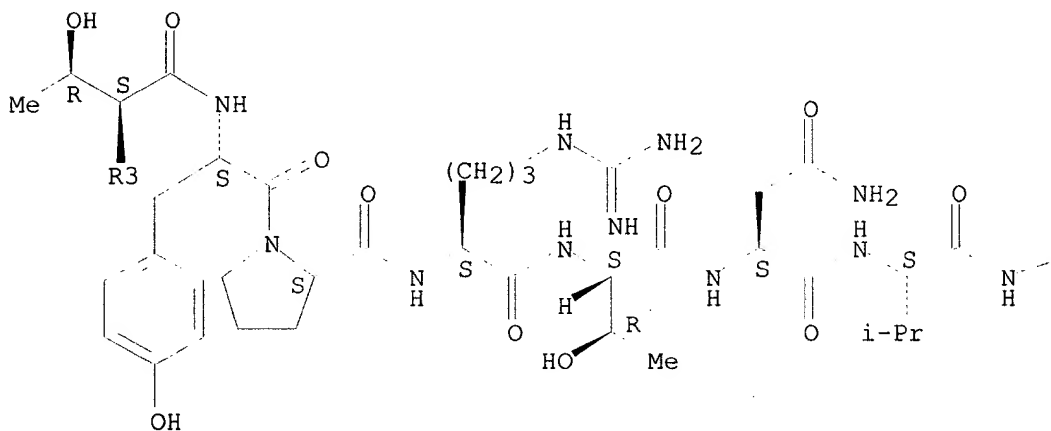


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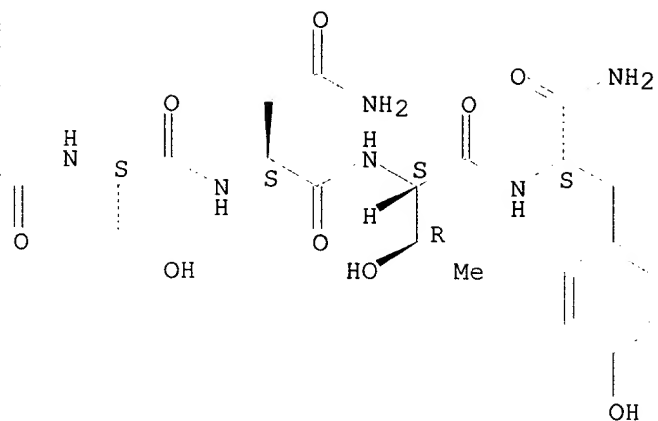
CN L-Tyrosinamide, N-acetyl-L-alanyl-L-threonyl-L-glutaminy-L-arginyl-L-leucyl-L-alanyl-L-asparaginy-L-glutaminy-L-leucyl-L-valyl-L-arginyl-L-leucyl-L-glutaminy-L-threonyl-L-tyrosyl-L-prolyl-L-arginyl-L-threonyl-L-asparaginy-L-valylglycyl-L-seryl-L-asparaginy-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

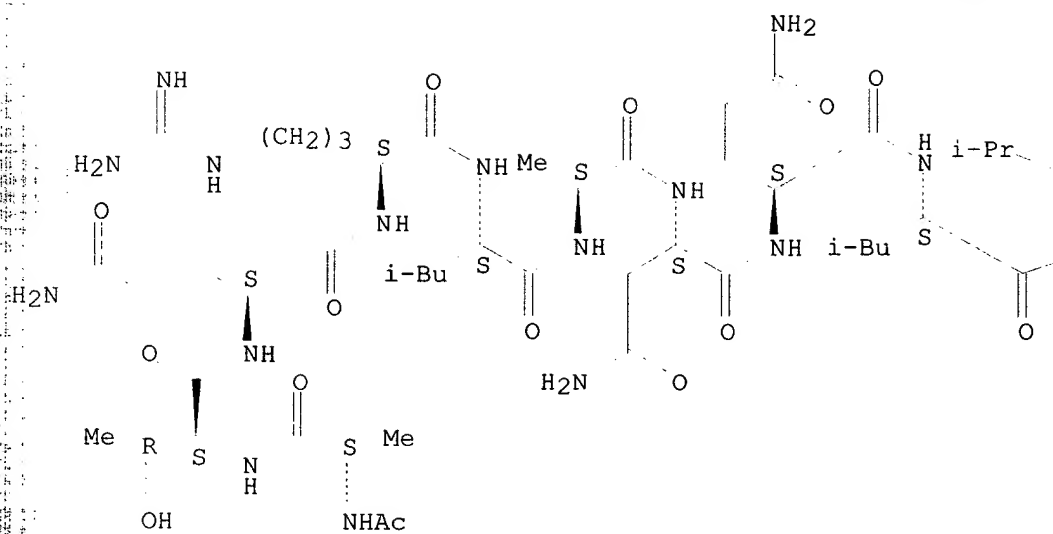
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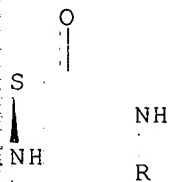
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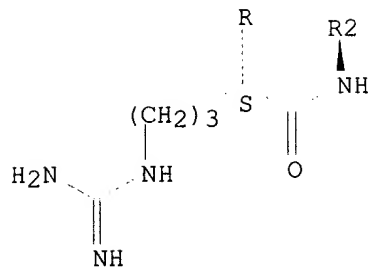
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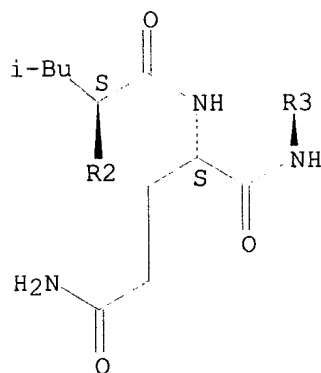
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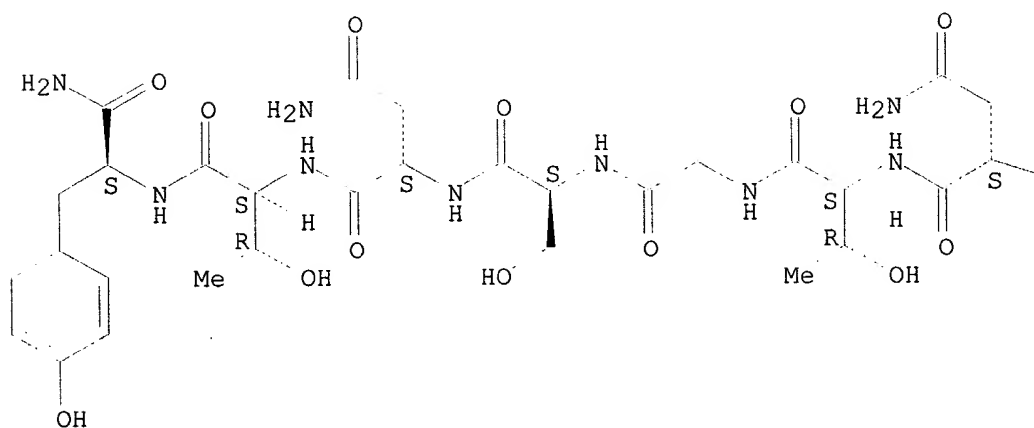
PAGE 4-A



RN 184581-35-9 CAPLUS
CN 9-32-Calcitonin (salmon reduced), N-acetyl-30-L-asparagine-32-L-tyrosinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

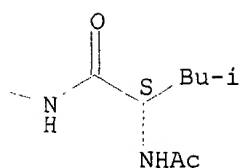
PAGE 1-A



[illegible]

Chemical structure of the repeating unit of poly(2,5-bis(4-aminobenzoyl)thiophene) (PABT) is shown, featuring a central thiophene ring substituted with two 4-aminobenzoyl groups. The structure includes labels for the repeating unit, the amine group (NH₂), the carbonyl group (CO₂H), and the thiophene ring. The structure is drawn in a perspective view, showing the spatial arrangement of the atoms and bonds.

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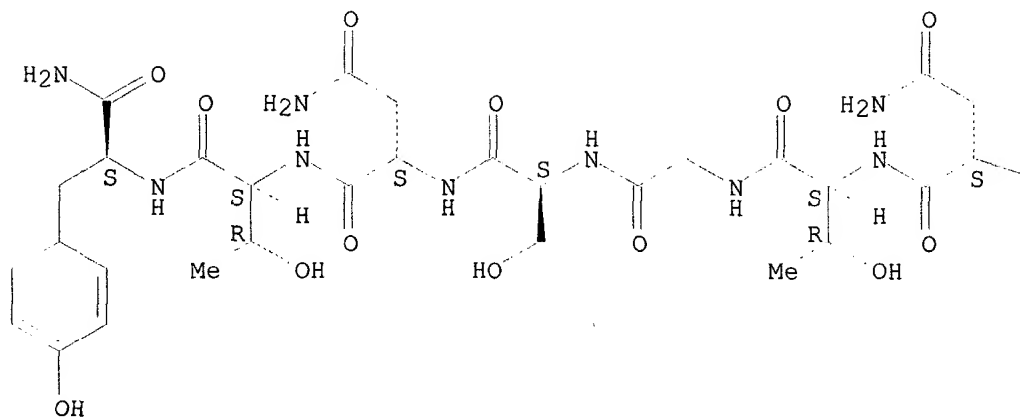


RN 184581-36-0 CAPLUS

CN 9-32-Calcitonin (salmon reduced), N-acetyl-11-L-arginine-30-L-asparagine-32-L-tyrosinamide- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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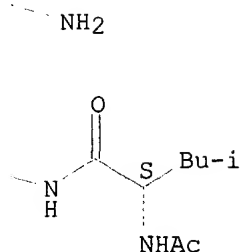


Chemical structures of various thiocarbonyl compounds:

- Thioamide: NC(=S)R
- Thioester: NC(=O)SR
- Thioacetals: NC(=S)SR and NC(=S)SR2
- Thioamides with substituents: NC(=S)R (where R is a phenyl group, a 3-oxopropyl group, a 2-hydroxy-1-methylpropyl group, or an isobutyl group).

[illegible]

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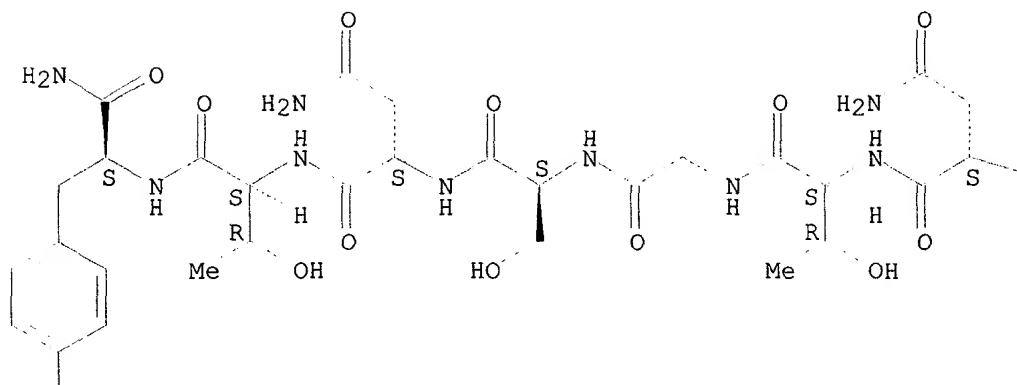


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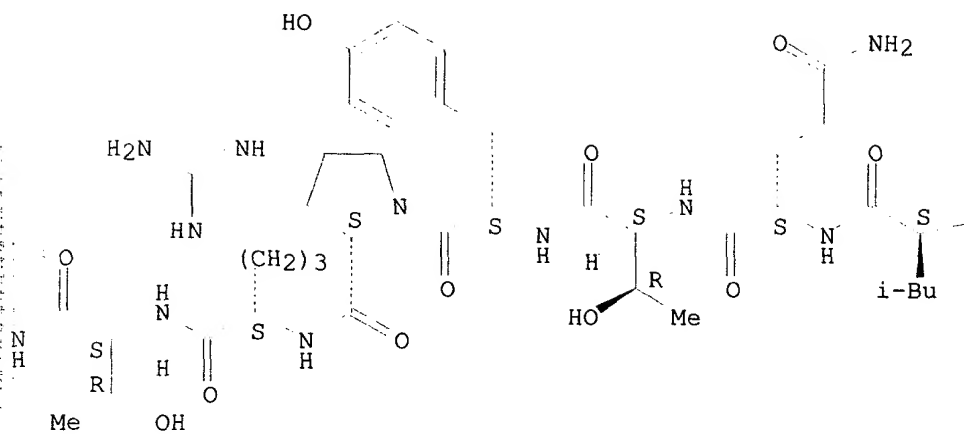
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threonyl-L-tyrosyl-L-prolyl-L-arginyl-L-threonyl-L-asparaginyl-L-
threonylglycyl-L-seryl-L-asparaginyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

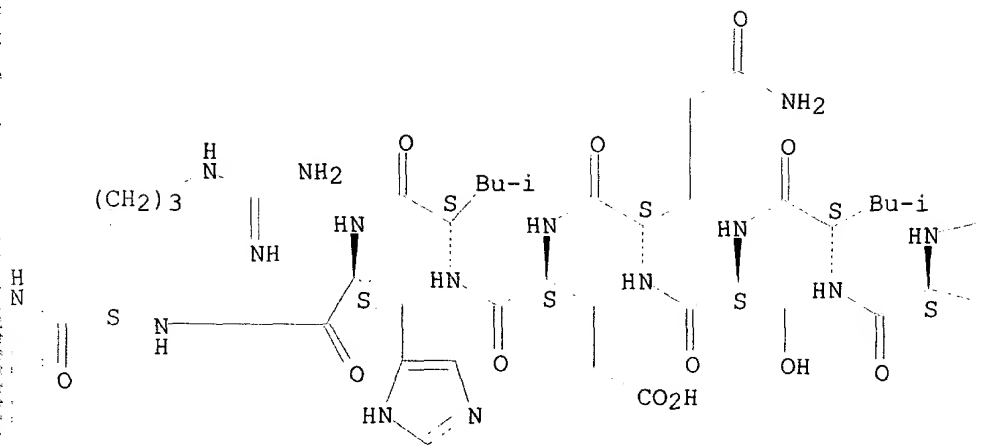
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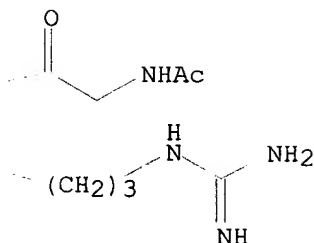
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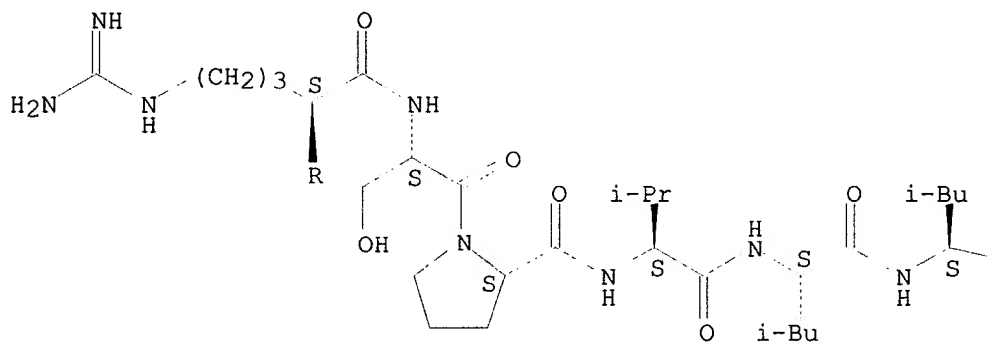
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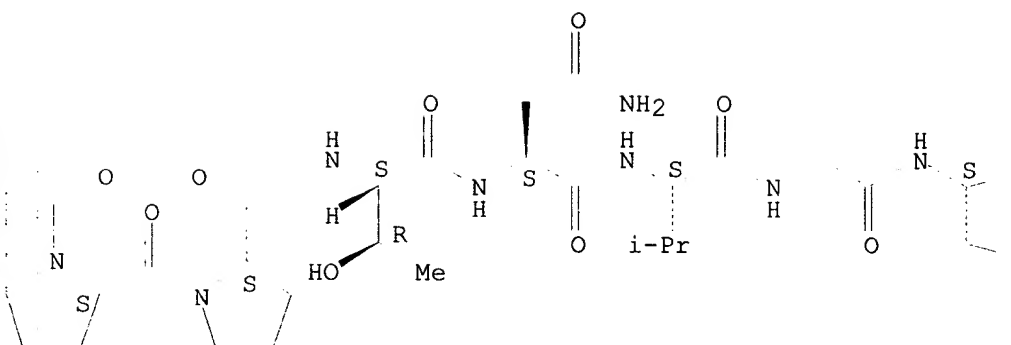
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Absolute stereochemistry.

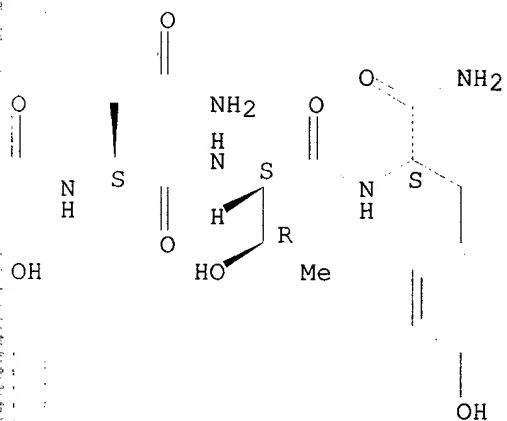
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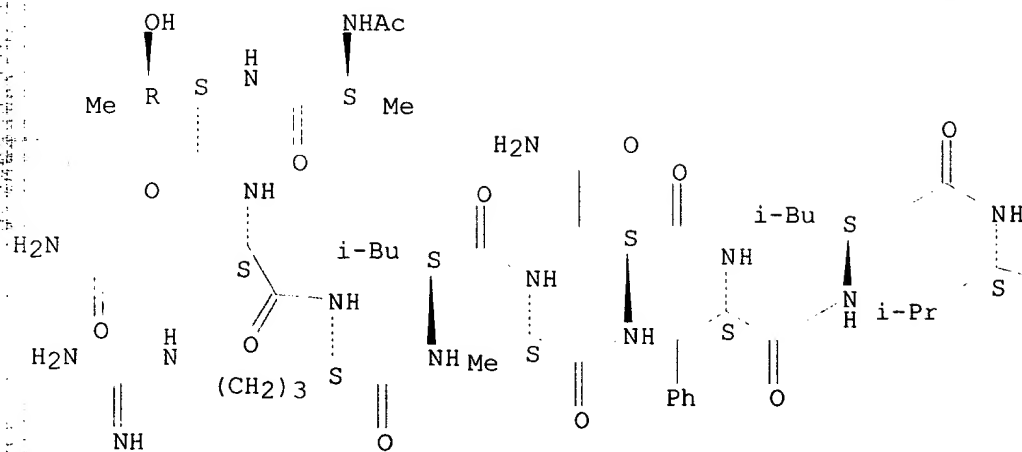
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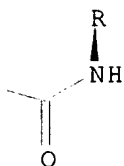
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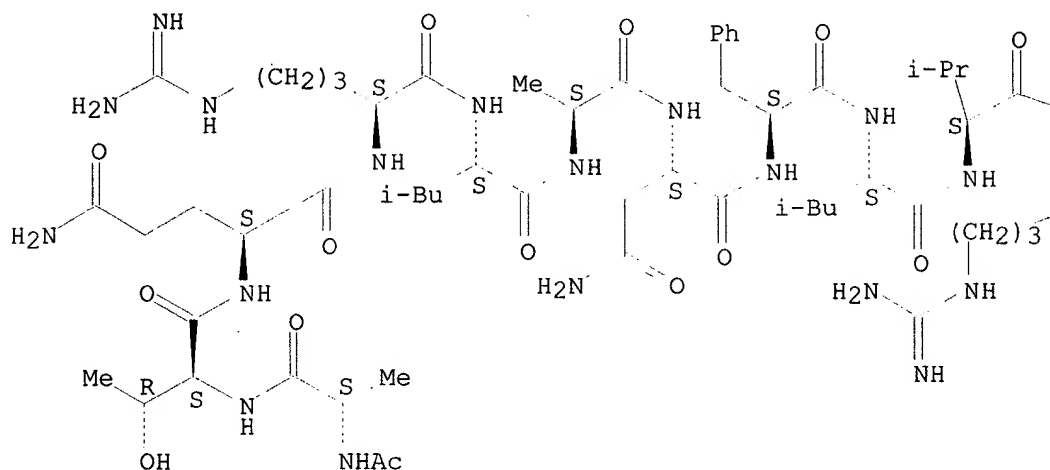


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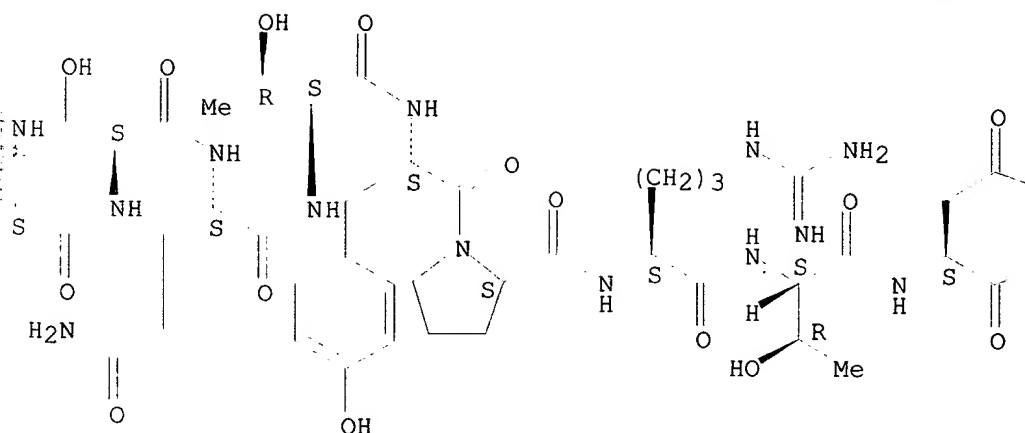
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Absolute stereochemistry.

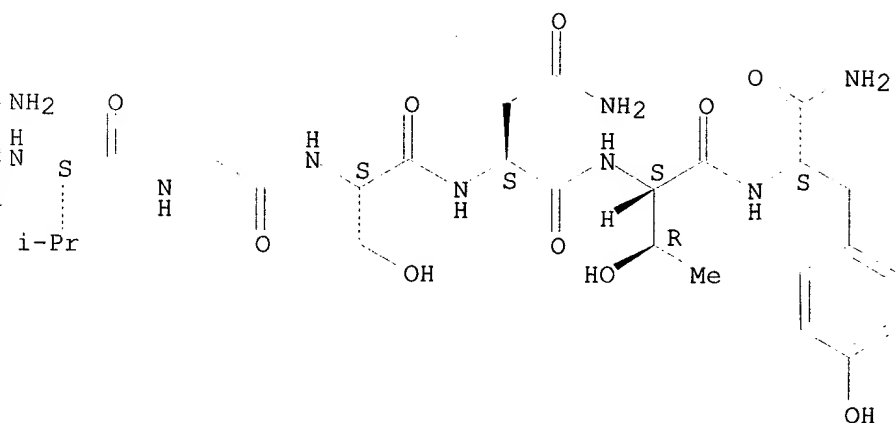
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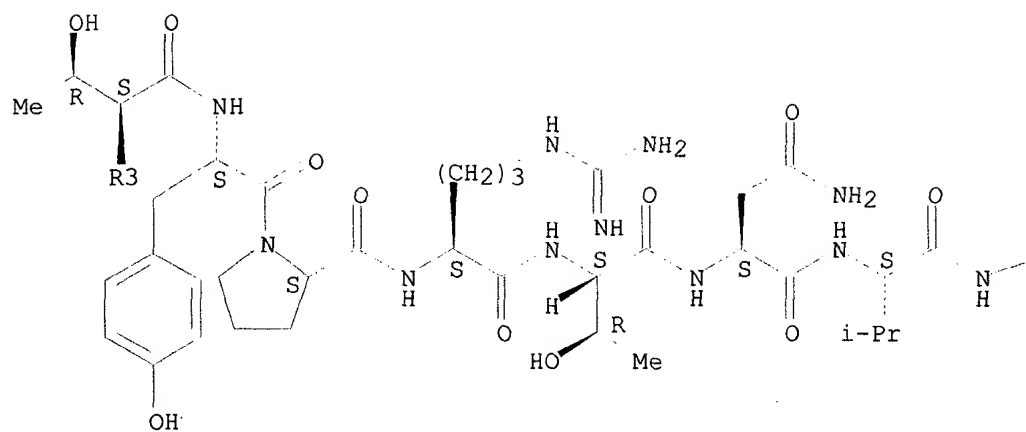
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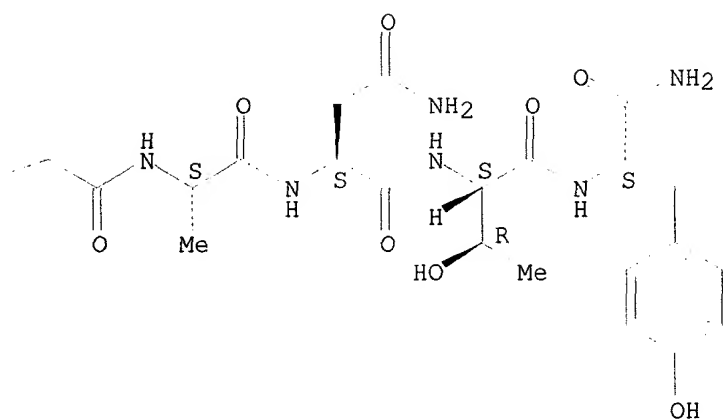
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Absolute stereochemistry.

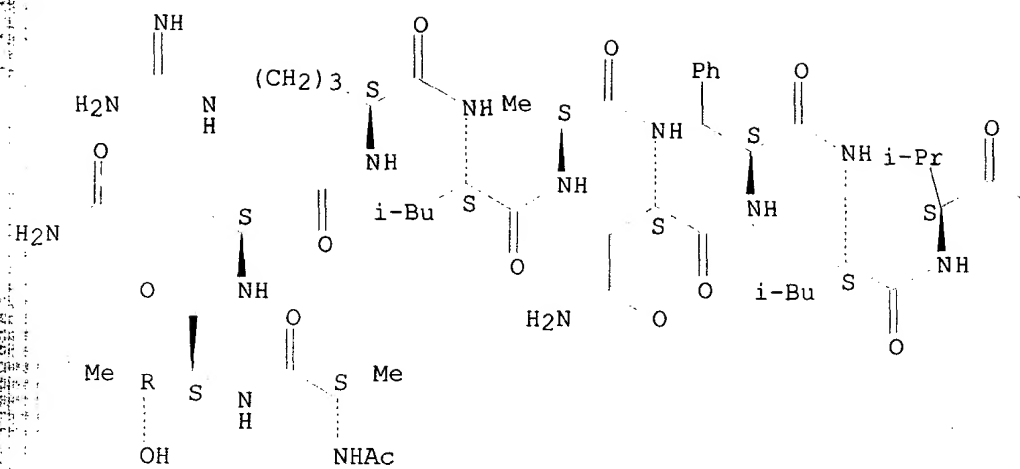
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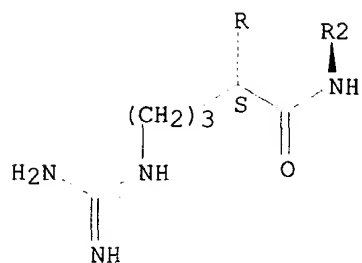
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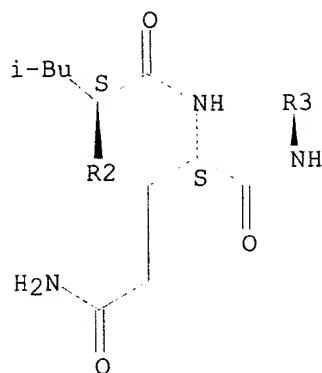
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NH
R

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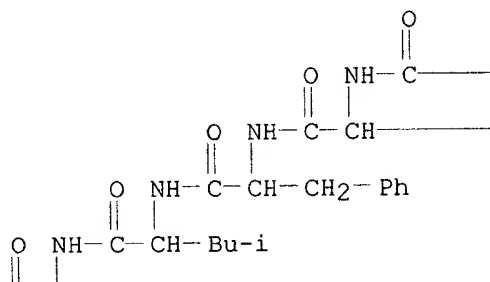


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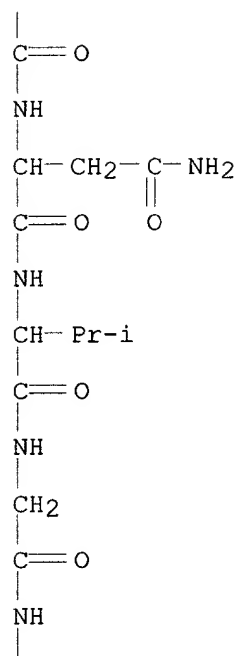
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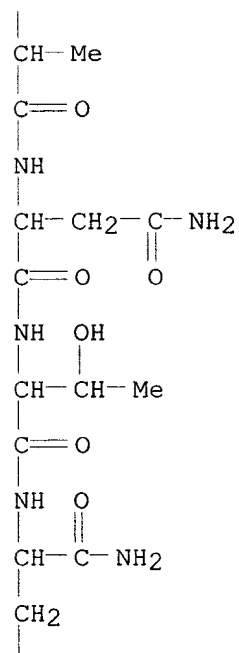


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 \text{NH} - \text{C}(=\text{O}) - \text{CH} - \text{CH}(\text{OH}) - \text{Me} \\
 | \\
 \text{NH} - \text{C}(=\text{O}) - \text{CH} - \text{CH}_2 - \text{CH}_2 - \text{C}(=\text{O}) - \text{NH}_2 \\
 | \\
 \text{NH} - \text{C}(=\text{O}) - \text{CH} - (\text{CH}_2)_3 - \text{NH} - \text{C}(=\text{O}) - \text{NH}_2 \\
 | \qquad \qquad \qquad | \\
 \text{NH} - \text{C}(=\text{O}) - \text{CH} - \text{Bu-i} \qquad \qquad \qquad \text{NH} \\
 | \\
 \text{CH} - \text{Me} \\
 | \\
 \text{CH}_2 - \text{C}(=\text{O}) - \text{NH}_2 \\
 | \\
 \text{O}
 \end{array}$$
$$\begin{array}{c}
 \text{OH} \\
 | \\
 \text{||} \\
 \text{CH}_2 \\
 | \\
 \text{CH}-\text{NH}-\text{C}(=\text{O})-\text{CH}-\text{CH}-\text{Me} \\
 | \qquad | \qquad | \\
 \text{C}=\text{O} \quad \text{OH} \\
 | \\
 \text{N} \quad \text{C}(=\text{O})-\text{NH}-\text{CH}-(\text{CH}_2)_3-\text{NH}-\text{C}(=\text{NH})-\text{NH}_2 \\
 | \\
 \text{C}=\text{O} \\
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 \text{NH} \quad \text{OH} \\
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 \text{CH}-\text{CH}-\text{Me}
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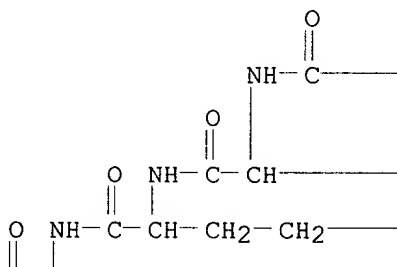
PAGE 4-A



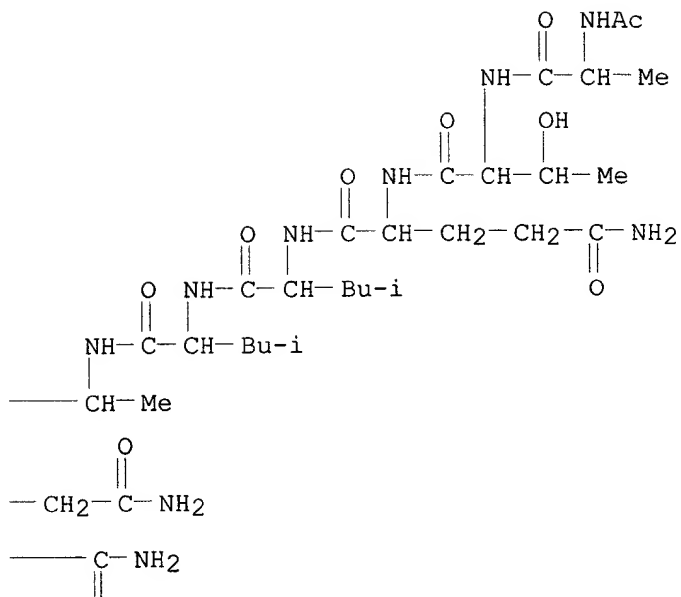
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L-Tyrosinamide, N-acetyl-L-alanyl-L-threonyl-L-glutaminyl-L-leucyl-L-leucyl-L-alanyl-L-asparaginyl-L-glutaminyl-L-leucyl-L-valyl-L-arginyl-L-leucyl-L-glutaminyl-L-threonyl-L-tyrosyl-L-prolyl-L-arginyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl- (9CI) (CA INDEX NAME)

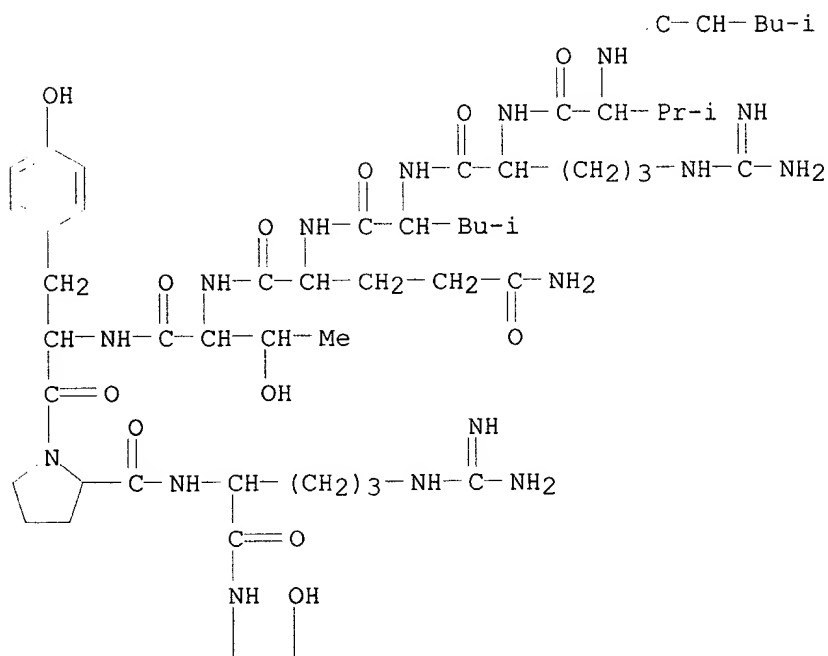
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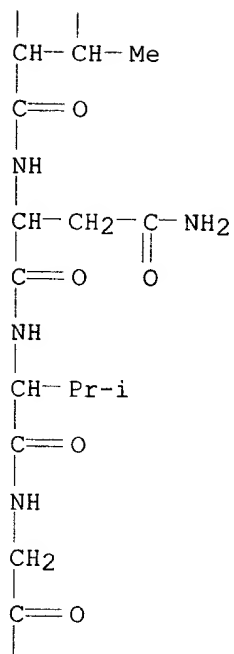
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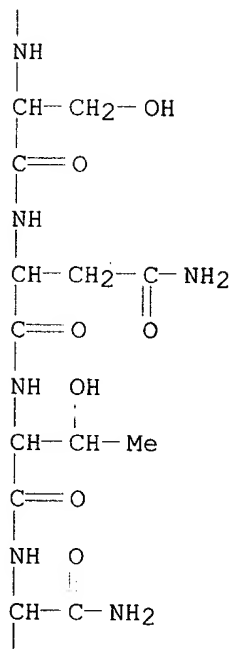
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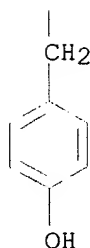
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L25 ANSWER 36 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:666998 CAPLUS

DOCUMENT NUMBER: 125:284978

TITLE: Use of a **calcitonin gene-related peptide antagonists** for the treatment of ocular or eyelid pruritus and dysesthesia

INVENTOR(S): De Lacharriere, Olivier; Breton, Lionel

PATENT ASSIGNEE(S): Oreal S. A., Fr.

SOURCE: Eur. Pat. Appl., 8 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 734730	A1	19961002	EP 1996-400459	19960304
EP 734730	B1	20010905		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2732222	A1	19961004	FR 1995-3629	19950328
FR 2732222	B1	19970425		
AT 205089	E	20010915	AT 1996-400459	19960304
ES 2163596	T3	20020201	ES 1996-400459	19960304
BR 9601461	A	19980331	BR 1996-1461	19960325
CA 2172779	AA	19960929	CA 1996-2172779	19960327
JP 08268913	A2	19961015	JP 1996-72774	19960327
JP 3024064	B2	20000321		
RU 2155601	C2	20000910	RU 1996-105819	19960327
US 6169069	B1	20010102	US 1996-623576	19960328
US 6344438	B1	20020205	US 2000-589117	20000608

PRIORITY APPLN. INFO.:

FR 1995-3629 A 19950328

US 1996-623576 A3 19960328

AB Pharmaceutical or cosmetic compns. contg. calcitonin gene-related peptide (CGRP) antagonists are used for the treatment of ocular or eyelid pruritus and dysesthesia. A collyrium contained CGRP 8-37 0.5, and excipients comprising sodium chloride, sodium borate, Polysorbate 80, boric acid and water q.s. 100%.

IT 119911-68-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified);

THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of **calcitonin gene-related**

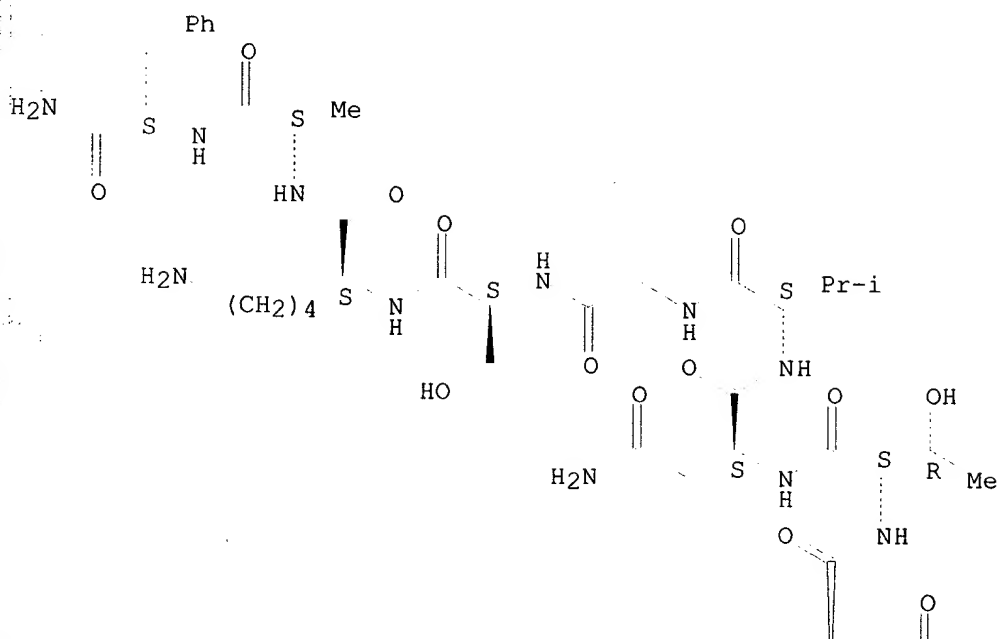
peptide antagonists for treatment of ocular or eyelid pruritus and dysesthesia)

RN 119911-68-1 CAPLUS

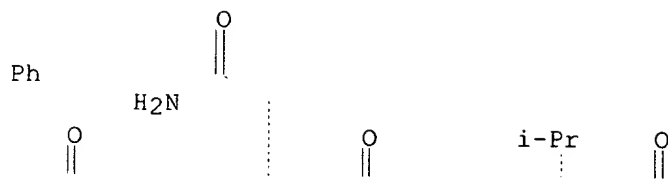
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



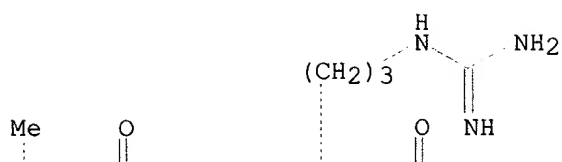
PAGE 1-B



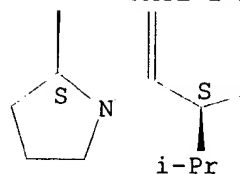
PAGE 1-C



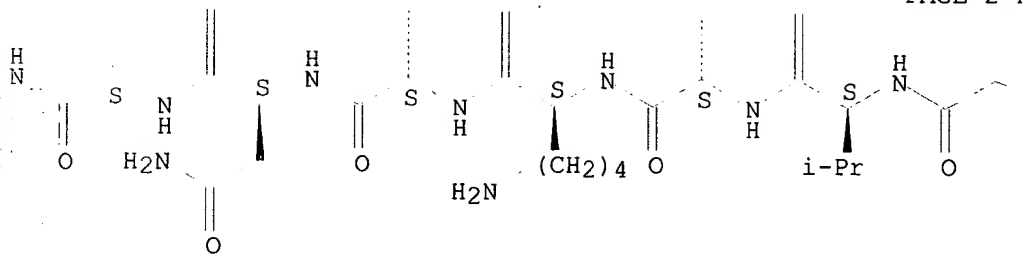
PAGE 1-D



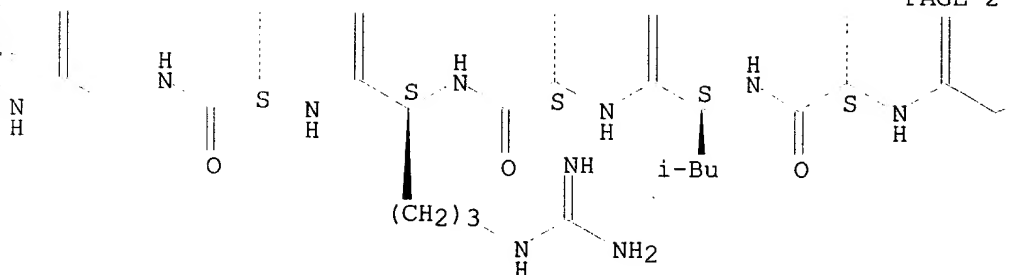
PAGE 2-A



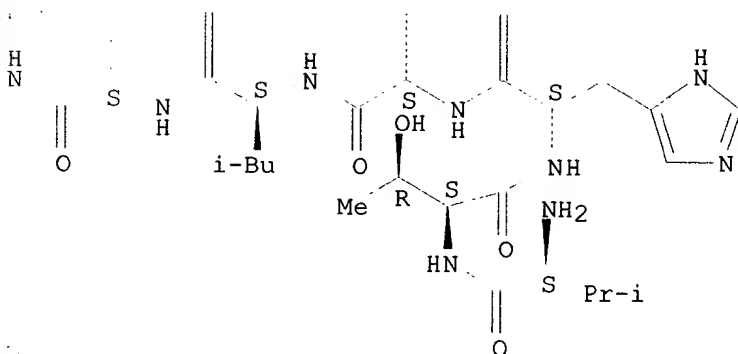
PAGE 2-B



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PAGE 2-D



L25 ANSWER 37 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:666997 CAPLUS
DOCUMENT NUMBER: 125:284977
TITLE: Use of a calcitonin gene-related peptide antagonists

Searched by Barb O'Bryen, STIC 308-4291

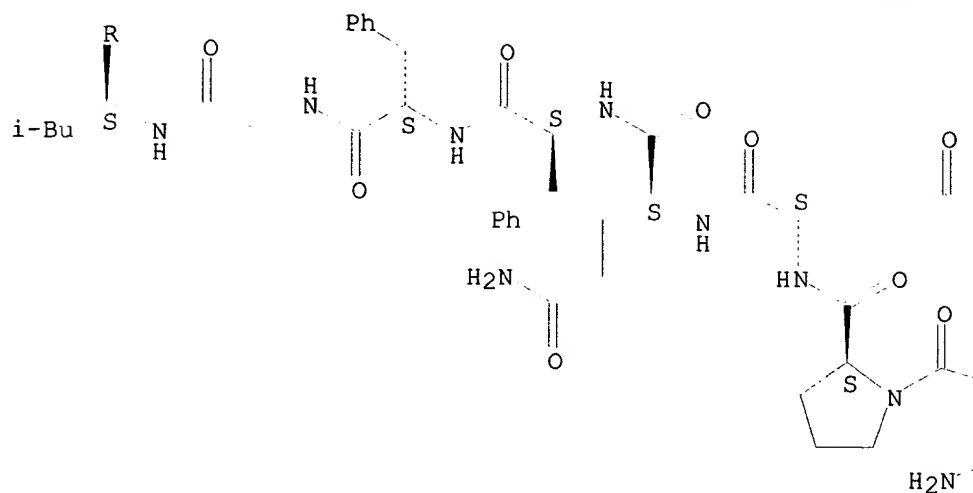
for the treatment of cutaneous erythema of neurogenic origin
INVENTOR(S): De Lacharriere, Olivier; Breton, Lionel
PATENT ASSIGNEE(S): Oreal S. A., Fr.
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 734729	A1	19961002	EP 1996-400457	19960304
EP 734729	B1	19980708		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2732221	A1	19961004	FR 1995-3628	19950328
FR 2732221	B1	19970425		
AT 168011	E	19980715	AT 1996-400457	19960304
ES 2121461	T3	19981116	ES 1996-400457	19960304
CA 2172777	AA	19960929	CA 1996-2172777	19960327
JP 08268874	A2	19961015	JP 1996-72773	19960327
BR 9601478	A	19980602	BR 1996-1478	19960327
RU 2152798	C1	20000720	RU 1996-105821	19960327
US 5932215	A	19990803	US 1996-620806	19960328

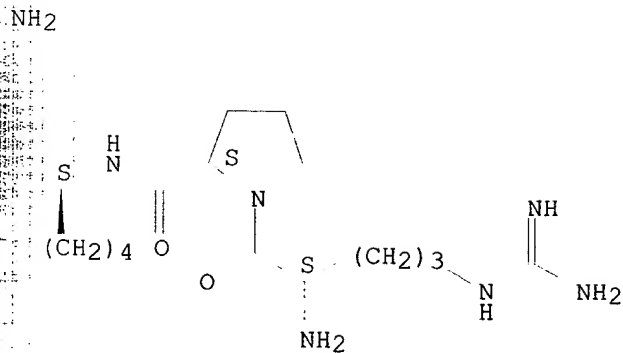
PRIORITY APPLN. INFO.: FR 1995-3628 A 19950328
AB Pharmaceutical and cosmetic compns. contg. calcitonin gene-related peptide (CGRP) antagonists are used for the treatment of cutaneous erythema of neurogenic origin. A cream contained CGRP 8-37 0.50, glycerol stearate 2, Polysorbate 60 1, stearic acid 1.4, triethanolamine 0.7, carbomer 0.4, cyclomethicone 8, sunflower oil 12, antioxidants 0.05, preservative 0.30, and water q.s. 100%.
IT 33507-63-0, Substance p
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (antagonists; use of calcitonin gene-related peptide antagonists for treatment of cutaneous erythema of neurogenic origin)
RN 33507-63-0 CAPLUS
CN Substance P (9CI) (CA INDEX NAME)

Absolute stereochemistry.

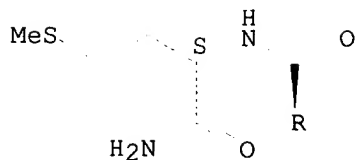
PAGE 1-A



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IT 119911-68-1
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); BUU (Biological use, unclassified);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (use of calcitonin gene-related

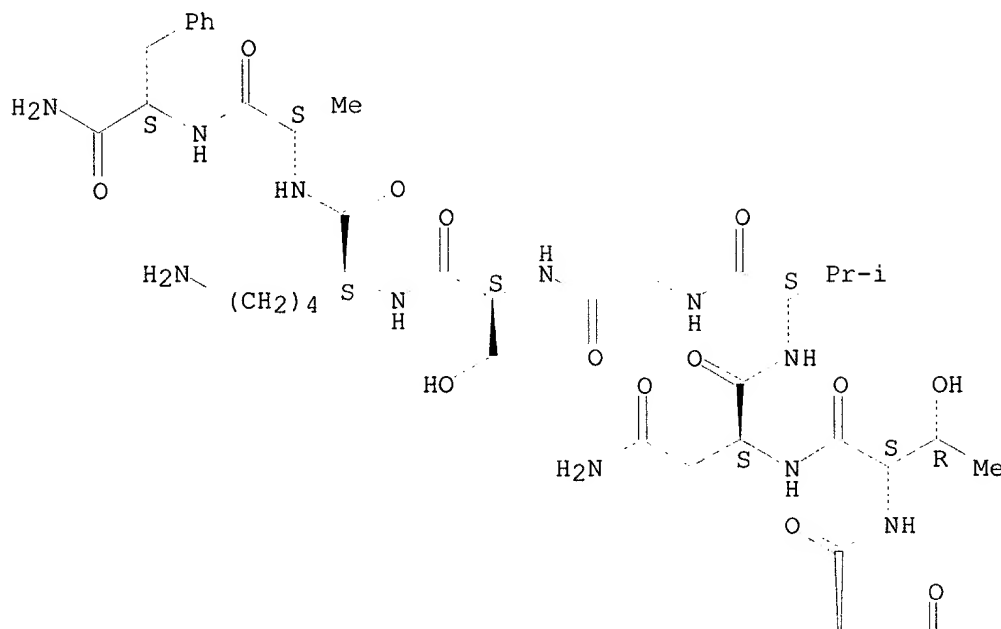
peptide antagonists for treatment of cutaneous
erythema of neurogenic origin)

RN 119911-68-1 CAPLUS

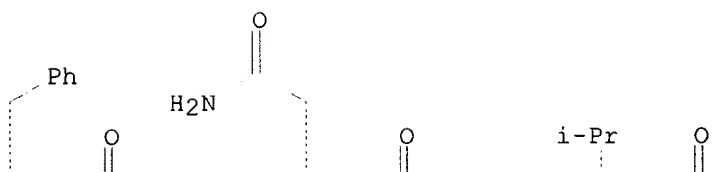
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

PAGE 1-A



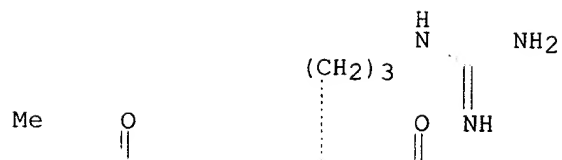
PAGE 1-B



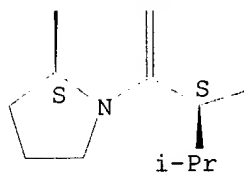
PAGE 1-C



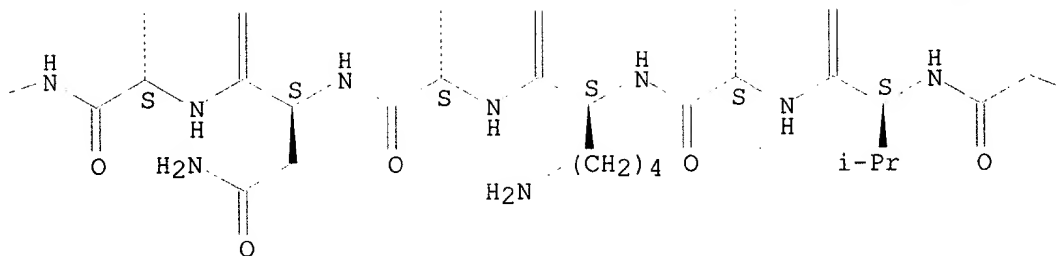
PAGE 1-D



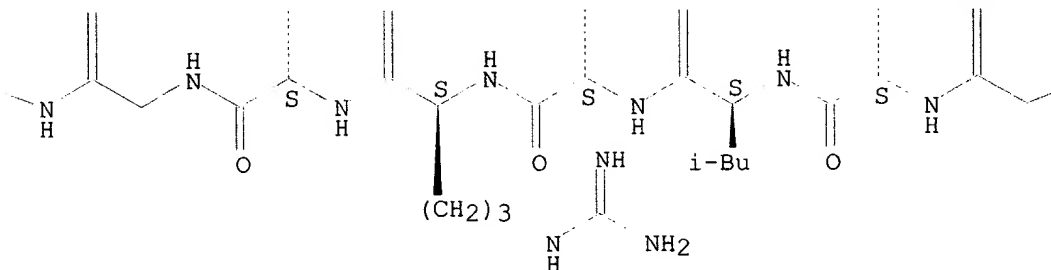
PAGE 2-A



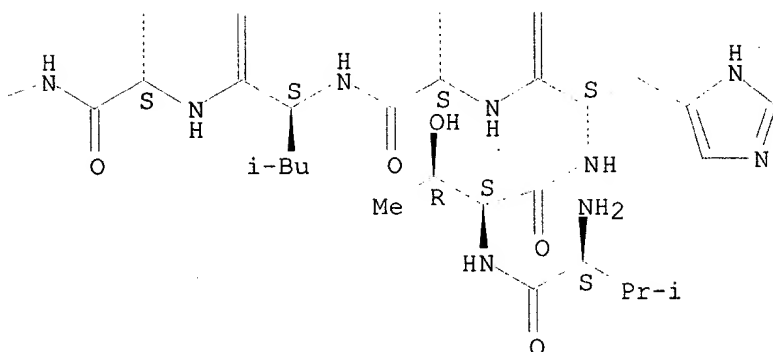
PAGE 2-B



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L25 ANSWER 38 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:666996 CAPLUS
DOCUMENT NUMBER: 125:284976
TITLE: Use of a calcitonin gene-related peptide antagonists

Searched by Barb O'Bryen; STIC 308-4291

for the treatment of lichens and pruritus
INVENTOR(S): De Lacharriere, Olivier; Breton, Lionel
PATENT ASSIGNEE(S): Oreal S. A., Fr.
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 734728	A1	19961002	EP 1996-400456	19960304
EP 734728	B1	20010606		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2732220	A1	19961004	FR 1995-3627	19950328
FR 2732220	B1	19970425		
ES 2159697	T3	20011016	ES 1996-400456	19960304
BR 9601467	A	19980331	BR 1996-1467	19960326
CA 2172778	AA	19960929	CA 1996-2172778	19960327
JP 08268904	A2	19961015	JP 1996-72772	19960327
JP 3043610	B2	20000522		
RU 2152785	C1	20000720	RU 1996-105824	19960327
US 5935586	A	19990810	US 1996-620805	19960328

PRIORITY APPLN. INFO.:

FR 1995-3627 A 19950328

AB Pharmaceutical and cosmetic compns. contg. calcitonin gene-related peptide (CGRP) antagonists are used for treatment of lichens and pruritus. A disinfectant lotion contained CGRP 8-37 0.50, antioxidants 0.05, isopropanol 40.00, preservative 0.30, isopropanol 40.0, preservative 0.30, and water q.s. 100%.

33507-63-0, Substance p

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

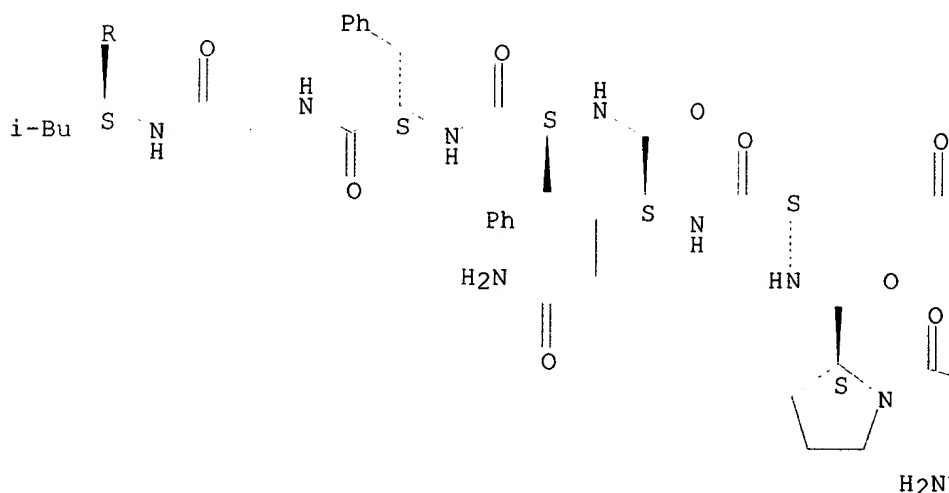
(antagonists; use of calcitonin gene-related peptide antagonists for treatment of lichens and pruritus)

RN 33507-63-0 CAPLUS

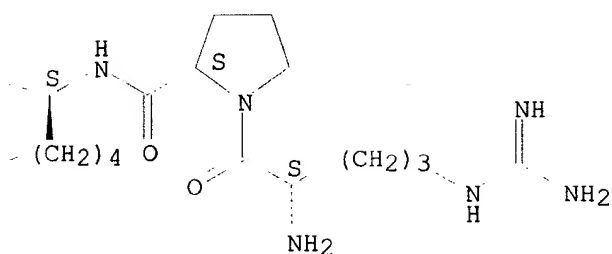
CN Substance P (9CI) (CA INDEX NAME)

Absolute stereochemistry.

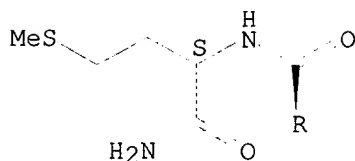
PAGE 1-A



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NH₂

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IT 119911-68-1

RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); BUU (Biological use, unclassified);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of calcitonin gene-related
peptide antagonists for treatment of lichens and
pruritus)

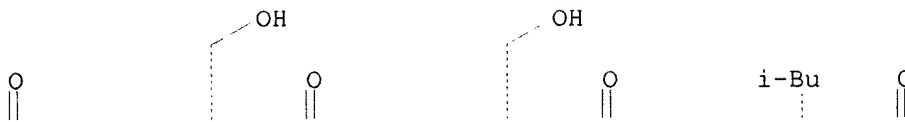
RN 119911-68-1 CAPLUS

CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX
NAME)

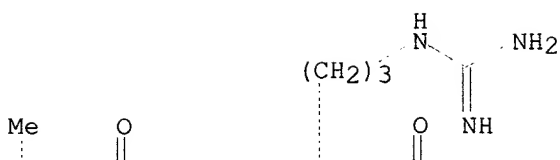
Absolute stereochemistry.

[illegible]O=C(Oc1ccccc1)C(=O)NCC(C)C

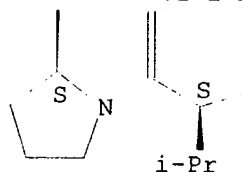
PAGE 1-C



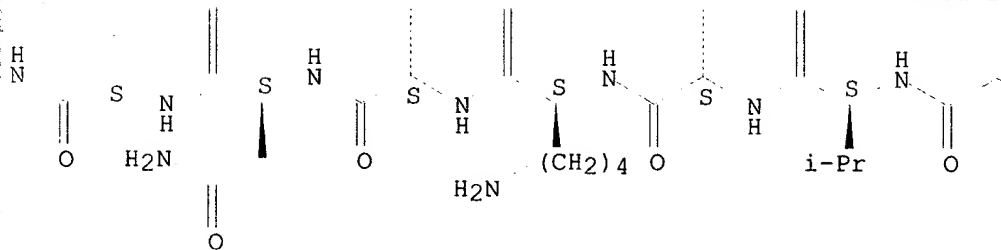
PAGE 1-D



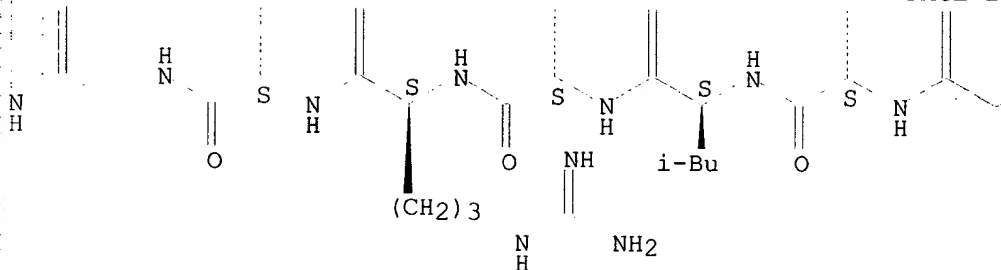
PAGE 2-A



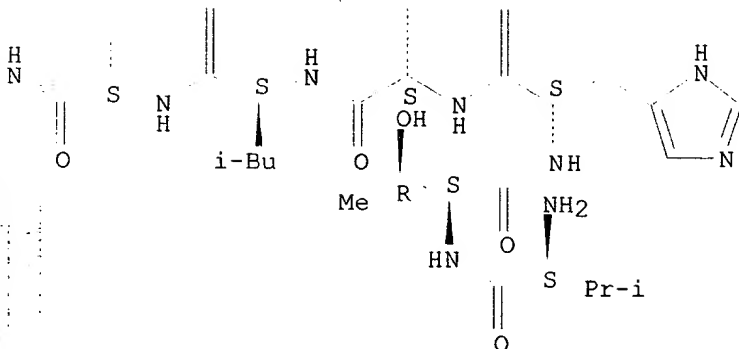
PAGE 2-B



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PAGE 2-D



L25 ANSWER 39 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:557876 CAPLUS

DOCUMENT NUMBER: 125:230186

TITLE: Cosmetic or pharmaceutical compositions comprising an antagonist of calcitonin

Searched by Barb O'Bryen, STIC 308-4291

INVENTOR(S): **gene related peptide**
Breton, Lionel; De Lacharriere, Olivier
PATENT ASSIGNEE(S): Oreal S. A., Fr.
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 723774	A1	19960731	EP 1996-400007	19960102
EP 723774	B1	20001206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2729855	A1	19960802	FR 1995-900	19950126
FR 2729855	B1	19970221		
AT 197896	E	20001215	AT 1996-400007	19960102
ES 2154388	T3	20010401	ES 1996-400007	19960102
BR 9600487	A	19980303	BR 1996-487	19960119
CA 2167980	AA	19960727	CA 1996-2167980	19960124
JP 08231434	A2	19960910	JP 1996-11284	19960125
JP 3043608	B2	20000522		
US 6019967	A	20000201	US 1996-592529	19960126
US 2001051157	A1	20011213	US 1999-429562	19991028
US 6416760	B2	20020709		

PRIORITY APPLN. INFO.: FR 1995-900 A 19950126
US 1996-592529 A3 19960126

AB The title compns. are claimed for prevention or treatment of skin disorders, such as irritation or dry skin. A lotion contained calcitonin gene related peptide 8-37 0.5, antioxidant 0.05, isopropanol 40.00, preservative 0.30, and water q.s. 100%.

IT **119911-68-1**

RL: BUU (Biological use, unclassified); THU (Therapeutic use);
BIOL (Biological study); USES (Uses)
(cosmetic or pharmaceutical compns. comprising an antagonist of calcitonin gene related peptide)

RN 119911-68-1 CAPLUS

CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

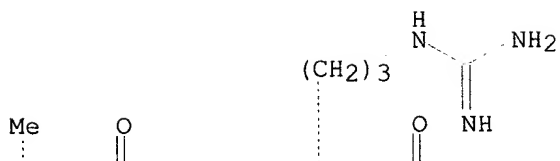
Absolute stereochemistry.

[illegible]CC(C)C(=O)NCC(=O)Cc1ccccc1

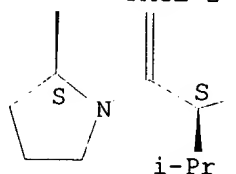
PAGE 1-C



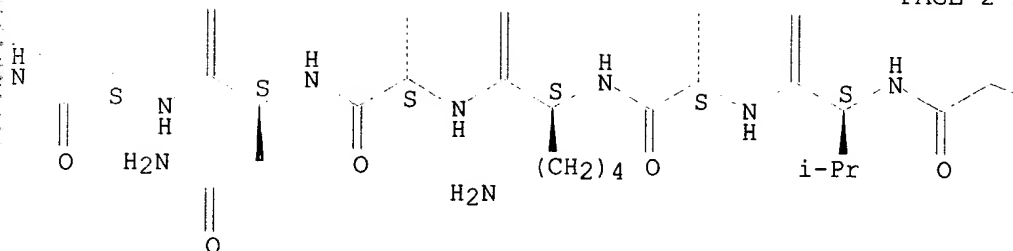
PAGE 1-D



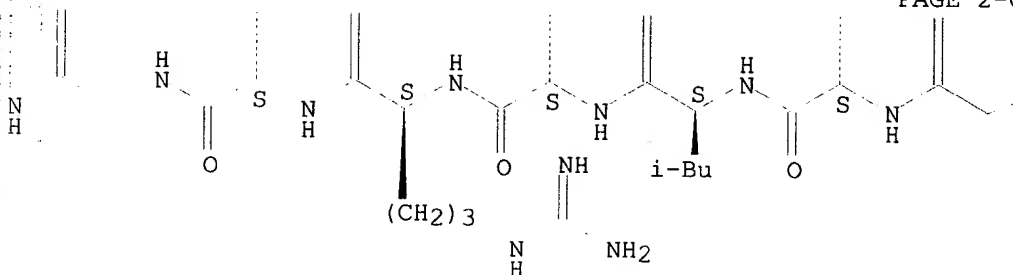
PAGE 2-A



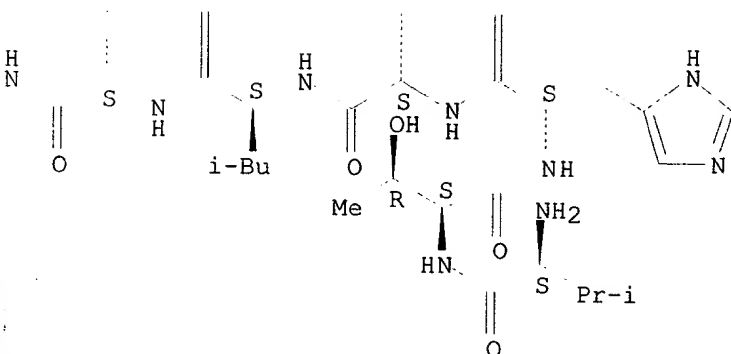
PAGE 2-B



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L25 ANSWER 40 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:485816 CAPLUS

DOCUMENT NUMBER: 125:123722

TITLE: Irrigation solution and method for inhibition of pain, inflammation and spasm

Searched by Barb O'Bryen, STIC 308-4291

INVENTOR(S): Demopoulos, Gregory A.; Pierce, Pamela Anne; Herz, Jeffrey M.
 PATENT ASSIGNEE(S): Omeros Medical Systems, Inc., USA
 SOURCE: PCT Int. Appl., 59 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 8
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9619233	A2	19960627	WO 1995-US16028	19951212
WO 9619233	A3	19960919		
W:	AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CA 2206119	AA	19960627	CA 1995-2206119	19951212
AU 9644673	A1	19960710	AU 1996-44673	19951212
EP 799051	A2	19971008	EP 1995-943396	19951212
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE			
CN 1175213	A	19980304	CN 1995-197538	19951212
BR 9509985	A	19981103	BR 1995-9985	19951212
CA 2240256	AA	19970619	CA 1996-2240256	19960626
WO 9721445	A1	19970619	WO 1996-US10954	19960626
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9663974	A1	19970703	AU 1996-63974	19960626
CN 1209066	A	19990224	CN 1996-199973	19960626
EP 910397	A1	19990428	EP 1996-923473	19960626
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 2000501729	T2	20000215	JP 1997-522011	19960626
NO 9702687	A	19970807	NO 1997-2687	19970611
US 6242447	B1	20010605	US 1998-72843	19980504
US 6261279	B1	20010717	US 1998-72913	19980504
US 6254585	B1	20010703	US 1998-109885	19980702
US 6210394	B1	20010403	US 1998-177671	19981022
US 6413961	B1	20020702	US 1999-388837	19990901
US 2001044616	A1	20011122	US 2001-837141	20010417
US 6420432	B2	20020716		
US 2002028798	A1	20020307	US 2001-839633	20010420
PRIORITY APPLN. INFO.:			US 1994-353775	A 19941212
			WO 1995-US16028	W 19951212
			US 1996-670699	A1 19960626
			WO 1996-US10954	W 19960626
			US 1998-72913	A2 19980504
			US 1998-109885	A1 19980702
			US 1998-98977P	P 19980902
			US 1998-105026P	P 19981020
			US 1998-105029P	P 19981020
			US 1998-105044P	P 19981020
			US 1998-105166P	P 19981021

US 1998-107256P P 19981105
WO 1999-US24557 A2 19991020
WO 1999-US24558 A2 19991020
WO 1999-US24625 A2 19991020
WO 1999-US24672 A2 19991020
WO 1999-US26330 A2 19991105

AB A method and a soln. for perioperatively inhibiting a variety of pain and inflammation and spasm processes at a wound, are provided. The soln. includes multiple pain and inflammation inhibitory agents and spasm inhibitory agents at dil. concn. in a physiol. base, such as saline or lactated Ringer's soln. Depending on the application, the soln. may include: (1) serotonin receptor antagonists; (2) serotonin receptor agonists; (3) histamine receptor antagonists; (4) bradykinin receptor antagonists; (5) kallikrein inhibitors; (6) tachykinin receptor antagonists, including neurokinin1 and neurokinin2 receptor subtype antagonists; (7) calcitonin gene-related peptide receptor antagonists; (8) interleukin receptor antagonists; (9) inhibitors of enzymes active in the synthetic pathway for arachidonic acid metabolites, including (a) phospholipase inhibitors, including PLA2 isoform and PLC.gamma. isoform inhibitors, (b) cyclooxygenase inhibitors, and (c) lipooxygenase inhibitors; (10) prostanoid receptor antagonists including eicosanoid EP-1 and EP-2 receptor subtype antagonists and thromboxane receptor subtype antagonists; (11) leukotriene receptor antagonists including leukotriene B4 and D4 receptor subtype antagonists; (12) opioid receptor agonists, including .mu.-opiate, .delta.-opiate, and .kappa.-opiate receptor subtype antagonists; (13) purinoceptor agonists and antagonists including gP2x receptor antagonists and P2y receptor agonists; (14) ATP-sensitive potassium channel openers; and (15) calcium channel antagonists. Suitable anti-inflammatory/anti-pain agents which also act as anti-spasm agents include serotonin receptor antagonists, tachykinin receptor antagonists, ATP-sensitive potassium channel openers and calcium channel antagonists. Other agents which may be utilized in the soln. specifically for their anti-spasm properties including endothelin receptor antagonists and the nitric oxide donors (enzyme activators). The soln. is used to continuously irrigate a wound during an operative/interventional procedure for preemptive inhibition of pain and inflammation, as well as vascular and smooth muscle spasm, while avoiding undesirable side effects assocd. with oral, i.m. or i.v. application of larger doses of the agents. The soln. is useful for arthroscopic, intravascular and urol. procedures, as well as for application to burns, and intra- and postoperative application to surgical wounds.

IT 129623-01-4, GR 82334

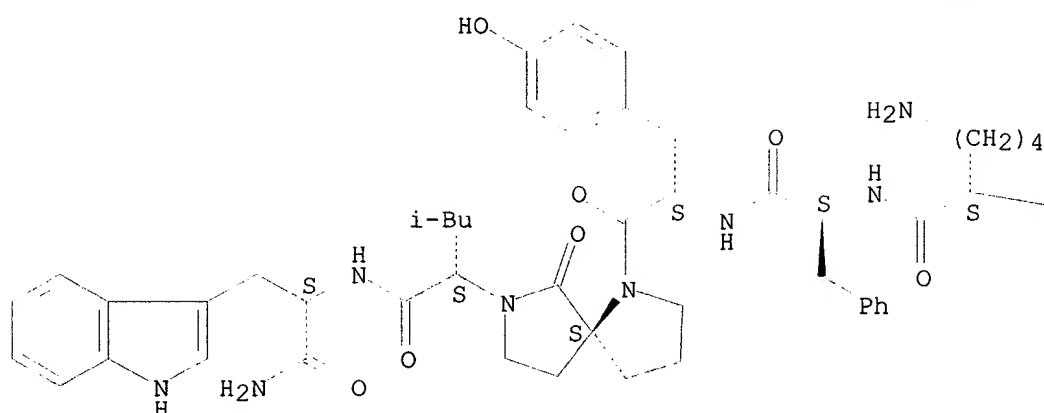
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irrigation soln. for inhibition of pain and inflammation and spasm)

RN 129623-01-4 CAPLUS

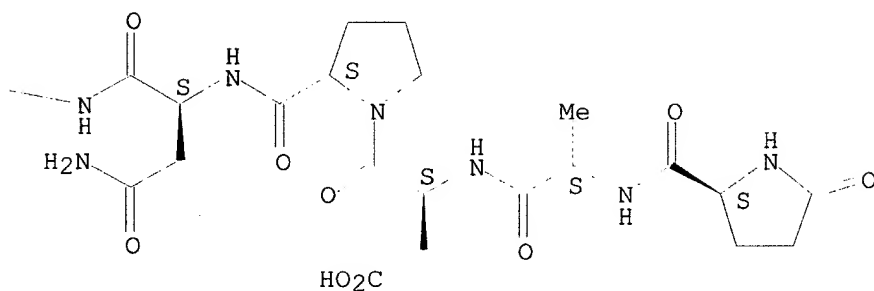
CN L-Tryptophanamide, 5-oxo-L-prolyl-L-alanyl-L-.alpha.-aspartyl-L-prolyl-L-asparaginyll-L-lysyl-L-phenylalanyl-L-tyrosyl-(.alpha.S,5S)-.alpha.-(2-methylpropyl)-6-oxo-1,7-diazaspiro[4.4]nonane-7-acetyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L25 ANSWER 41 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:460645 CAPLUS

DOCUMENT NUMBER: 125:133042

TITLE: Structural comparison of alanine-substituted analogs of the **calcitonin gene-related peptide 8-37**: importance of the C-terminal segment for **antagonistic** activity

AUTHOR(S): Boulanger, Y.; Khat, A.; Larocque, A.; Fournier, A.; St-Pierre, S.

CORPORATE SOURCE: INRS-Sante, Univ. Quebec, Quebec, Can.

SOURCE: International Journal of Peptide & Protein Research (1996), 47(6), 477-483

CODEN: IJPPC3; ISSN: 0367-8377

PUBLISHER: Munksgaard

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Replacement of specific residues of the antagonistic fragment human calcitonin gene-related peptide 8-37 (hCGRP 8-37) by alanine residues produces good antagonists to CGRP1 receptors when the replacement is made at positions 17 and 20 but a poor antagonist when the replacement is made at position 21. The soln. structures of hCGRP 8-37 and of the three

alanine analogs have been detd. by two-dimensional ^1H NMR spectroscopy and mol. modeling. Following the complete assignment of the NMR spectra, a comparison of the chem. shifts and of the temp. dependence of the amide chem. shifts showed that these parameters differed for [Ala17]-hCGRP 8-37 and [Ala20]-hCGRP 8-37 relative to hCGRP 8-37 in the N-terminal and central segments but not in the C-terminal segment (residues 31-37). In the case of [Ala21]-hCGRP 8-37, differences were obsd. all along the chain. Mol. modeling calcns. were performed by distance geometry, simulated annealing and energy minimization using NOE distance constraints. Mol. models showed a structural homol. between [Ala17]-hCGRP 8-37, [Ala20]-hCGRP 8-37 and hCGRP 8-37 in the C-terminal segment Asn31-Phe37 as well as hydrogen bonding between Val28 and Asn31. These structural similarities are not obsd. with [Ala21]-hCGRP 8-37. Therefore, the structure of the C-terminal segment of hCGRP 8-37 appears to be crit. for antagonistic activity at CGRP1 receptors.

IT 119911-68-1, Human calcitonin gene-

related peptide 8-37 180049-36-9,

[Ala17]-hCGRP 8-37 180049-37-0, [Ala20]-hCGRP 8-37

180049-38-1, [Ala21]-hCGRP 8-37

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(calcitonin gene-related peptide

C-terminal segment configurational requirement for CGRP1

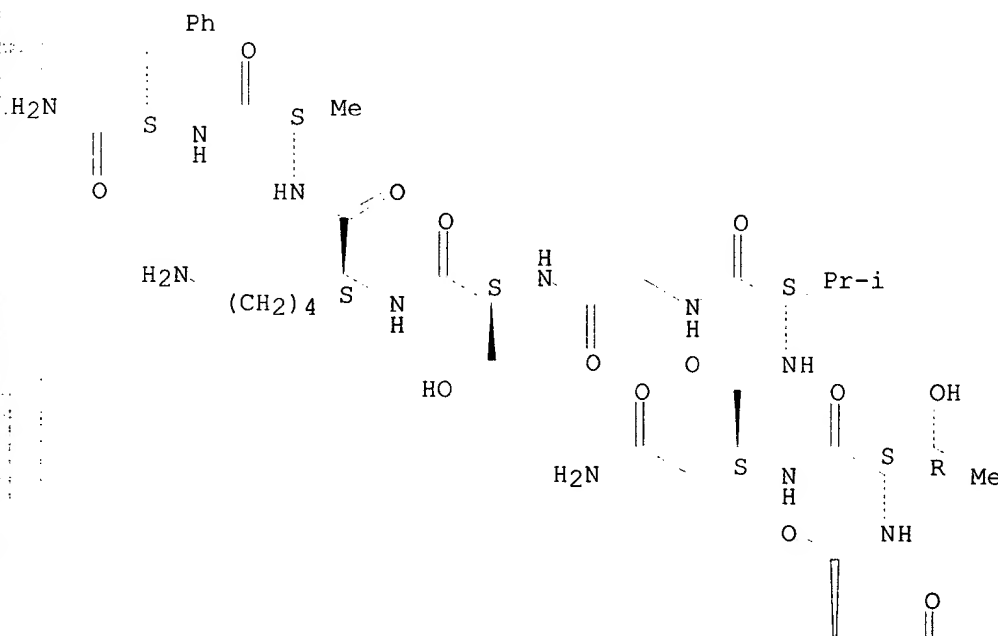
receptor antagonistic activity)

RN 119911-68-1 CAPLUS

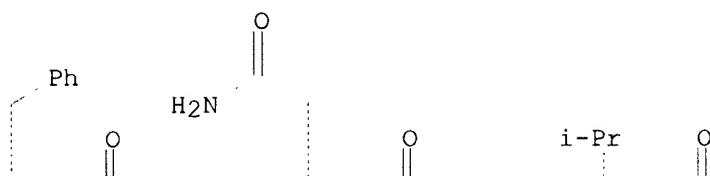
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



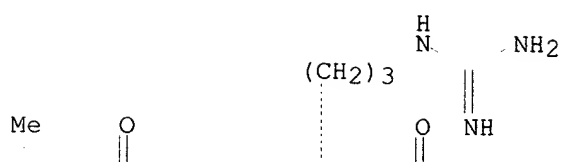
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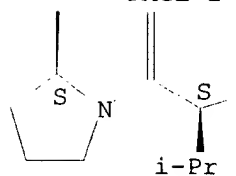
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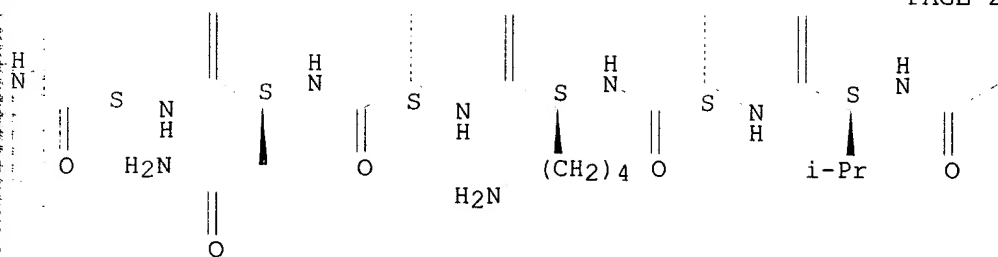
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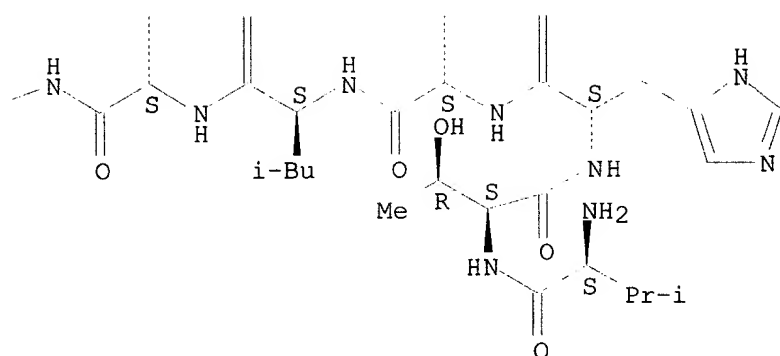
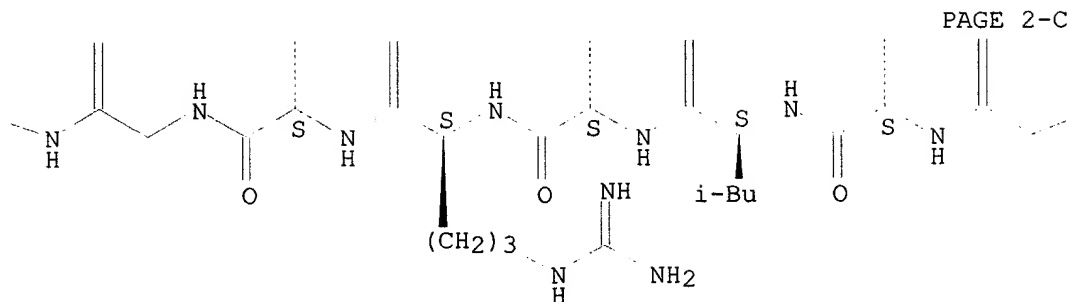


PAGE 2-A



PAGE 2-B

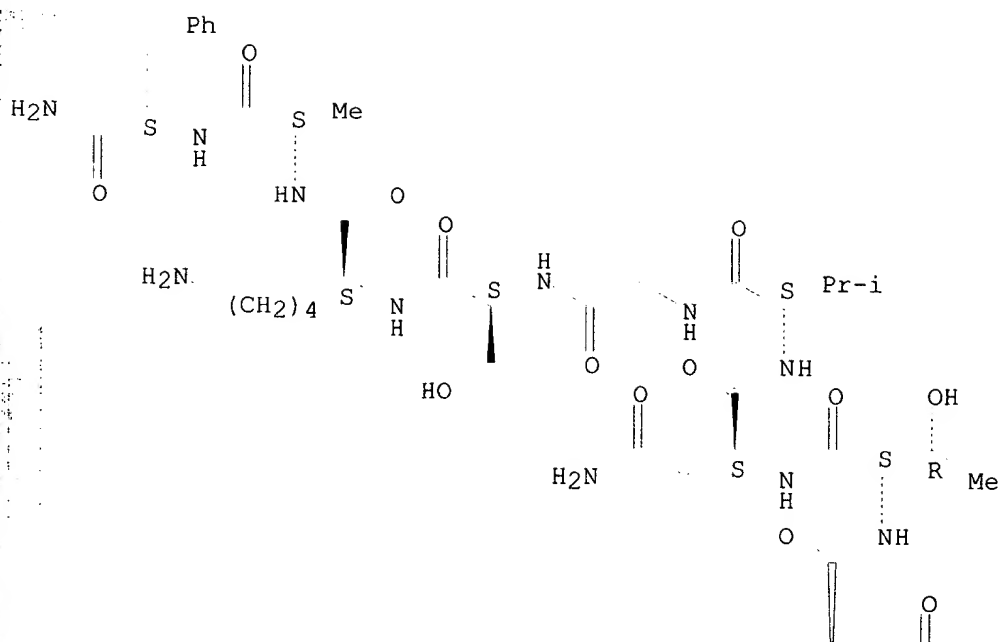




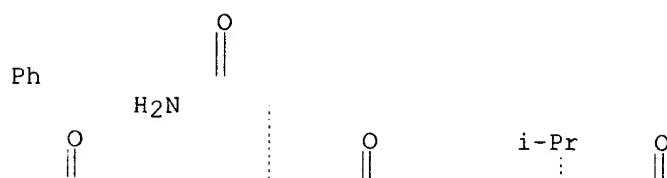
RN 180049-36-9 CAPLUS
CN 8-37-.alpha.-Calcitonin gene-related peptide (human reduced),
17-L-alanine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

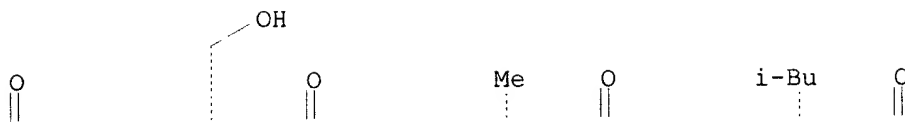
PAGE 1-A



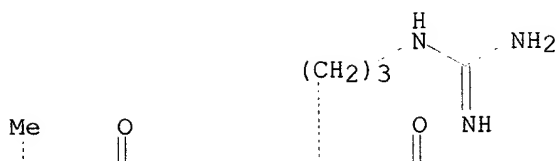
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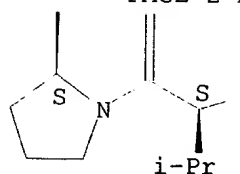
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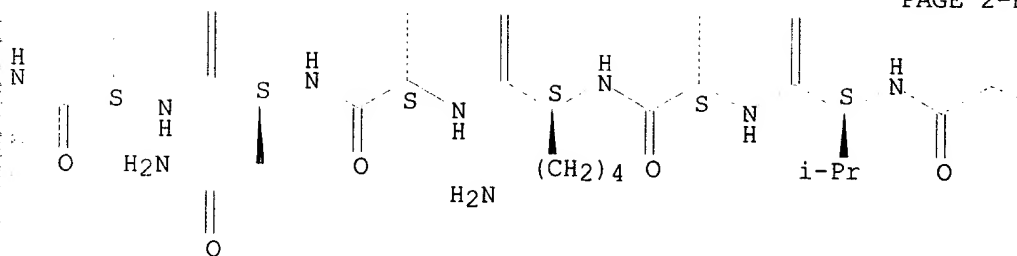
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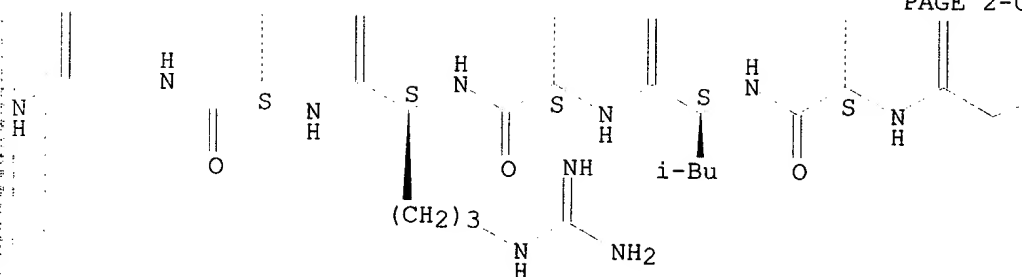
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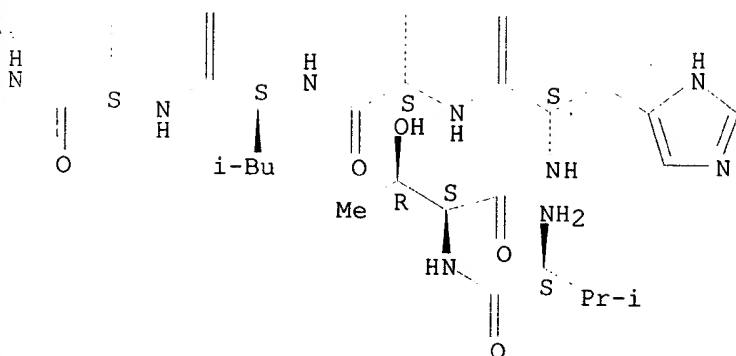
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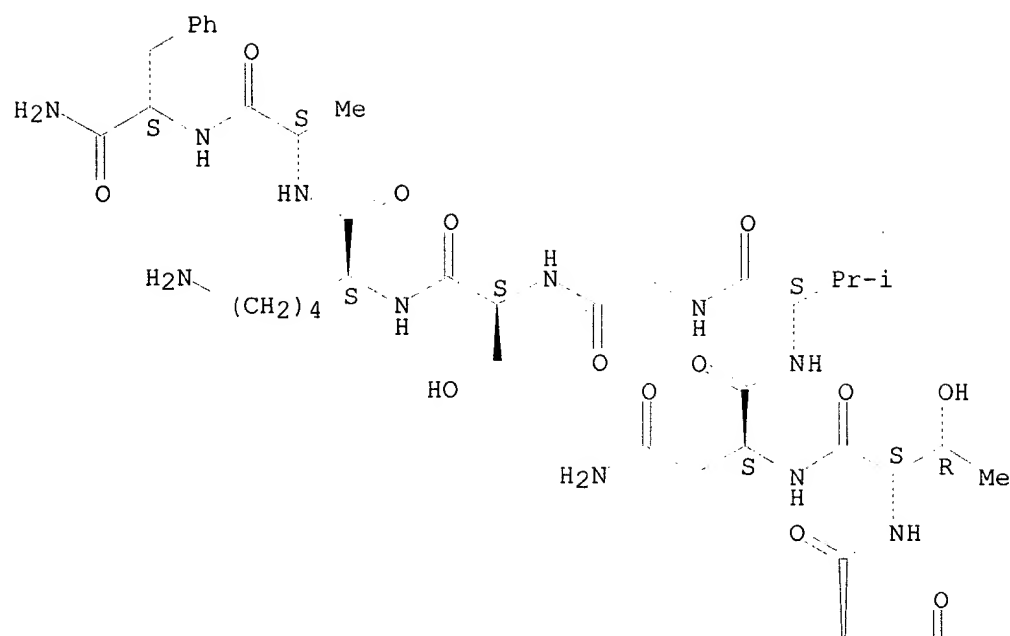
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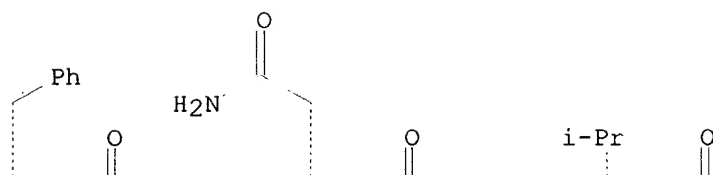
180049-37-0 CAPLUS
8-37-.alpha.-Calcitonin gene-related peptide (human reduced),
20-L-alanine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



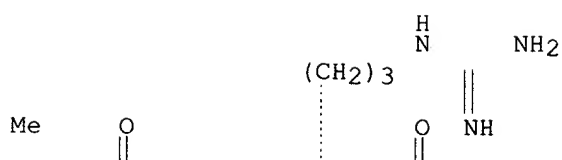
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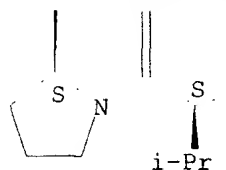
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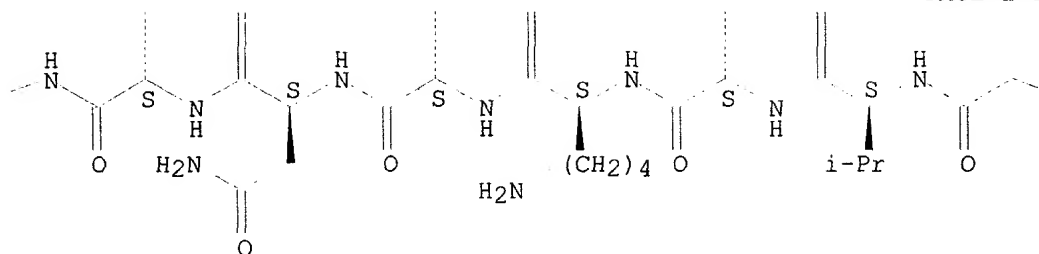
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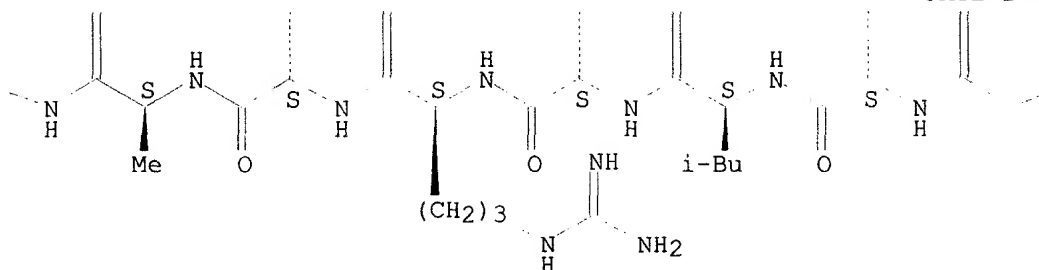
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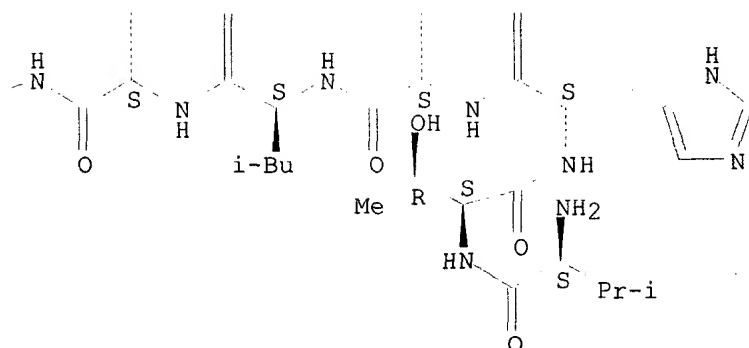
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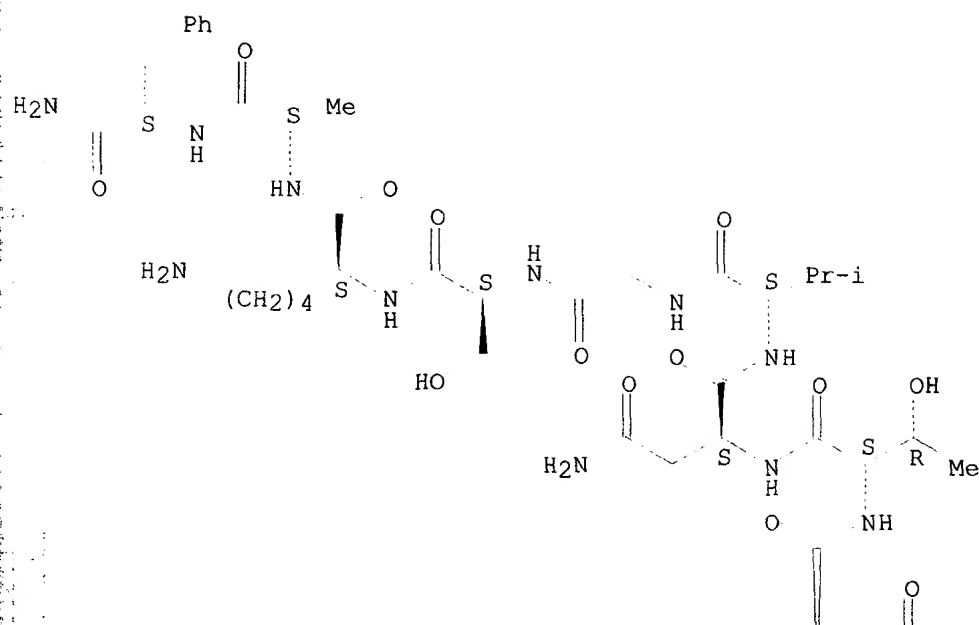
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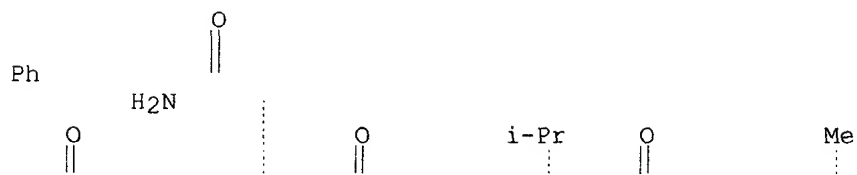
RN 180049-38-1 CAPLUS
 CN 8-37-.alpha.-Calcitonin gene-related peptide (human reduced),
 21-L-alanine- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



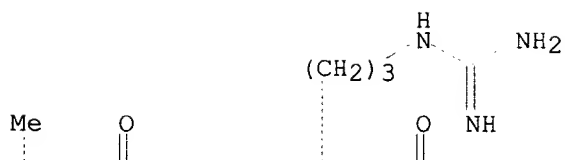
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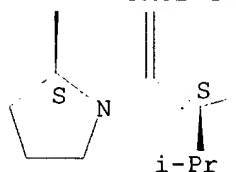
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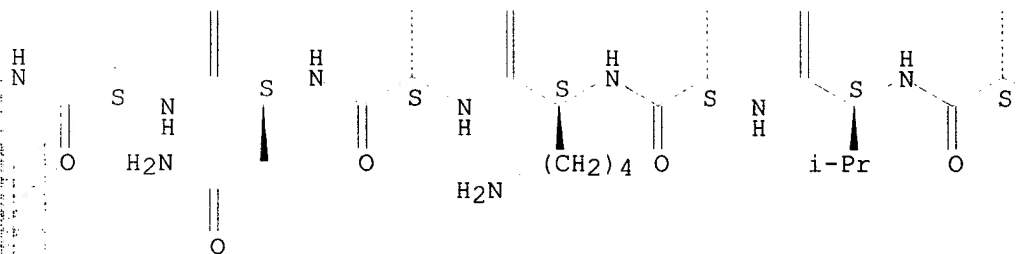
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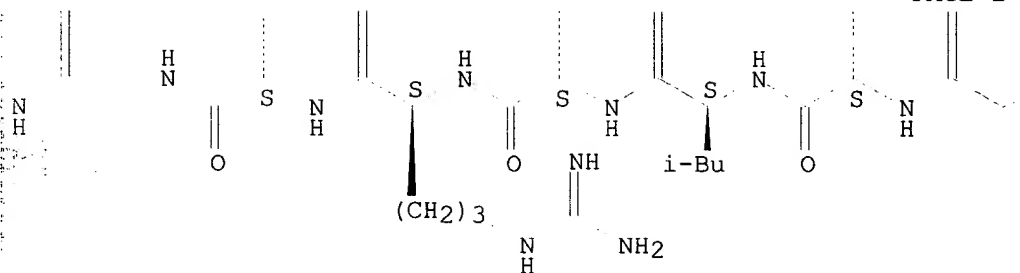
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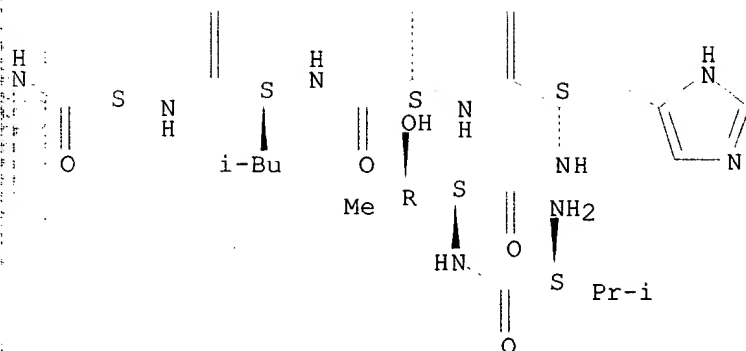
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125 ANSWER 42 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:184700 CAPLUS
DOCUMENT NUMBER: 124:221223
TITLE: A calcitonin gene-related
peptide receptor antagonist

prevents the development of tolerance to spinal morphine analgesia

AUTHOR(S): Menard, Daniel P.; van Rossum, Denise; Kar, S.; St. Pierre, S.; Sutak, M.; Jhamandas, K.; Quirion, Remi

CORPORATE SOURCE: Dep. Psychiatry Pharmacol. Therapeutics, McGill Univ., Verdun, PQ, H4H 1R3, Can.

SOURCE: J. Neurosci. (1996), 16(7), 2342-51
CODEN: JNRSDS; ISSN: 0270-6474

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Tolerance to morphine analgesia is believed to result from a neuronal adaptation produced by continuous drug administration, although the precise mechanisms involved have yet to be established. Recently, we reported selective alterations in rat spinal calcitonin gene-related peptide (CGRP) markers in morphine-tolerant animals. In fact, increases in CGRP-like immunostaining and decrements in specific [¹²⁵I]hCGRP binding in the superficial laminae of the dorsal horn were correlated with the development of tolerance to the spinal antinociceptive action of morphine. Other spinally located peptides such as substance P, galanin, and neuropeptide Y were unaffected. Thus, the major goal of the present study was to investigate whether the development of tolerance to spinally infused morphine could be modulated by the blockade of dorsal horn CGRP receptors using the potent CGRP antagonist hCGRP8-37. Indeed, cotreatments with hCGRP8-37 prevented, in a dose-dependent manner, the development of tolerance to morphine-induced analgesia in both the rat tail-flick/tail-immersion and paw-pressure tests. Moreover, alterations in spinal CGRP markers seen in morphine-tolerant animals were not observed after a coadministration of morphine and hCGRP8-37. These results demonstrate the existence of specific interaction between CGRP and the development of tolerance to the spinal antinociceptive effects of morphine. They also suggest that CGRP receptor antagonists could become useful adjuncts in the treatment of pain and tolerance to the antinociceptive effects of morphine.

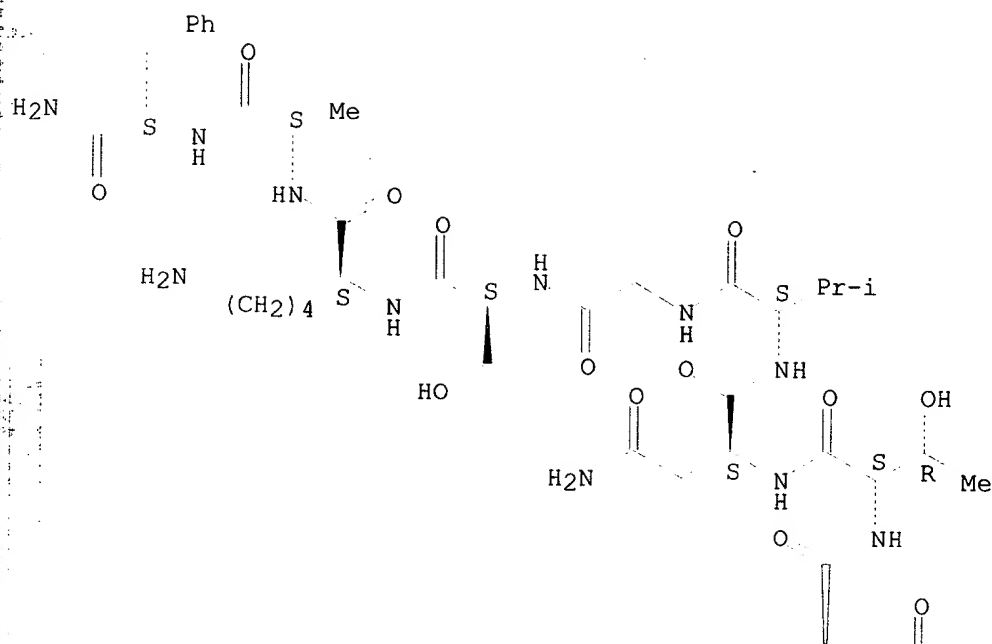
IT 119911-68-1, Human CGRP-8-37
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CGRP receptor antagonist prevents the development of tolerance to spinal morphine analgesia)

RN 119911-68-1 CAPLUS

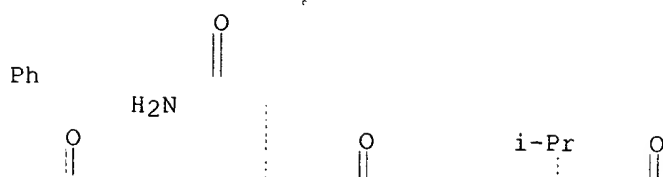
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



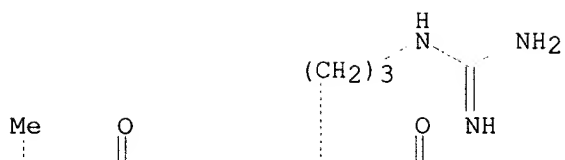
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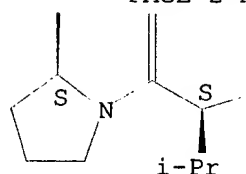
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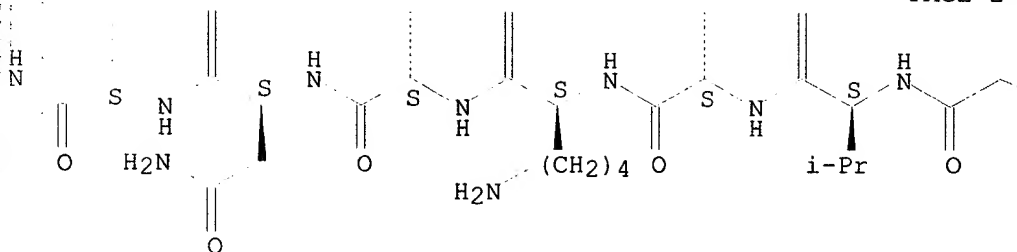
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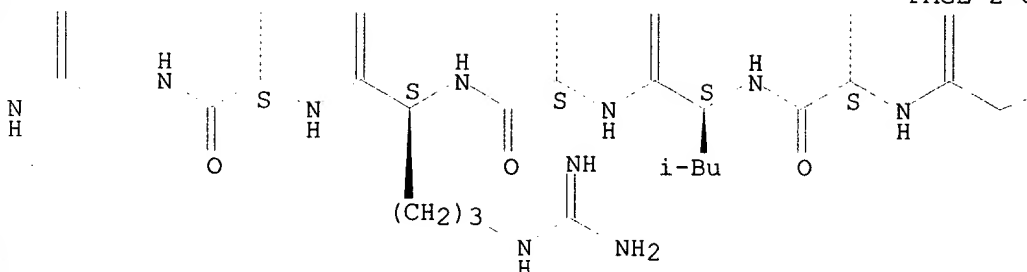
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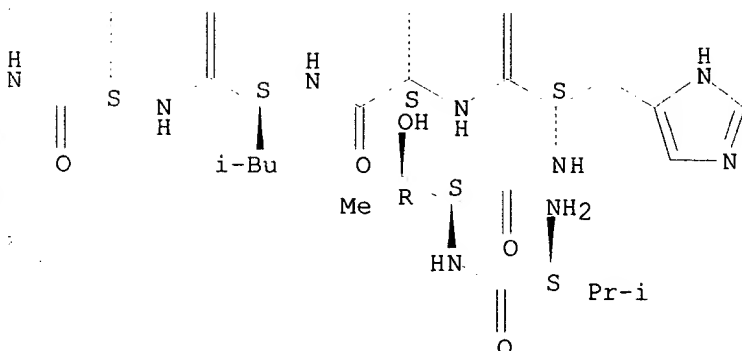
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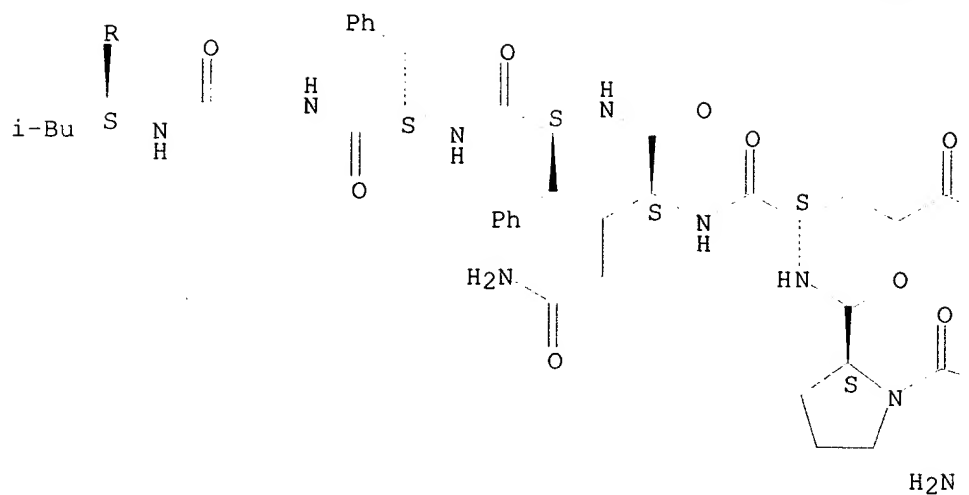
L25 ANSWER 43 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:170215 CAPLUS
DOCUMENT NUMBER: 124:220883
TITLE: Effects of hCGRP 8-37 and the NK1-receptor antagonist
SR 140.333 on capsaicin-evoked vasodilation in the pig

Searched by Barb O'Bryen, STIC 308-4291

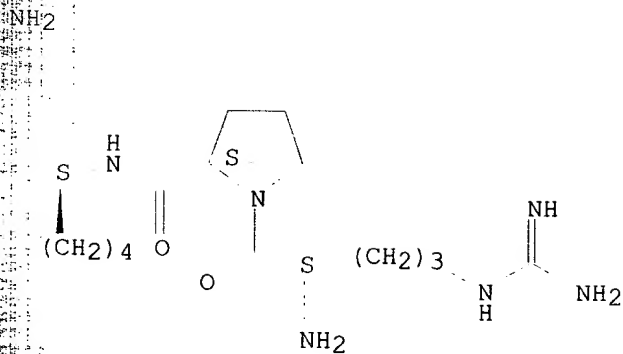
nasal mucosa in vivo
AUTHOR(S): Rinder, J.; Lundberg, J. M.
CORPORATE SOURCE: Dep. Physiol. Pharmacol., Div. Pharmacol., Stockholm, Swed.
SOURCE: Acta Physiol. Scand. (1996), 156(2), 115-22
CODEN: APSCAX; ISSN: 0001-6772
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel pig in vivo model was used to study vascular effects of capsaicin, substance P and calcitonin gene-related peptide (CGRP) in the nasal mucosa and skin. An acoustic rhinometer was used to measure changes in nasal cavity vol., mainly representing changes in capacitance vessels in the vascular beds. The non-peptide NK1-receptor antagonist SR 140.333 and the CGRP-receptor antagonist hCGRP 8-37 were used to investigate the role of substance P and CGRP, resp., in capsaicin-evoked vasodilation mediated through activation of sensory C-fiber afferents. In this study the authors show the SR 140.333 is a potent inhibitor of substance P-induced vasodilation in the nasal mucosa whereas it has no effect on the capsaicin-evoked responses. Substance P only elicited a minor and short-lasting increase in superficial skin blood flow; this response, however, was completely blocked after administration of SR 140.333. Capsaicin-evoked vasodilation in the skin was slightly reduced by Sr 140.333. CGRP-induced vasodilation in the nasal mucosa and skin was of much longer duration than the substance P-induced response, and was thus similar to the vascular effects mediated by capsaicin. hCGRP 8-37 significantly reduced both the CGRP- and capsaicin-mediated vasodilation in the nasal mucosa and the decrease of nasal cavity vol. Although the peak vasodilation in the skin in response to capsaicin, was unaltered by blockade of CGRP-receptors, the integrated response was significantly reduced by hCGRP 8-37. The present results show that vasodilatory responses to activation of afferent nerves in the pig nasal mucosa and superficial skin are mainly dependent on CGRP, while NK1-receptor mechanisms seem to be of no or minor importance.
IT 33507-63-0, Substance P (peptide)
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(effects of hCGRP 8-37 and the NK1-receptor antagonist SR 140.333 on capsaicin-evoked vasodilation in the pig nasal mucosa in vivo)
RN 33507-63-0 CAPLUS
CN Substance P (9CI) (CA INDEX NAME)

Absolute stereochemistry.

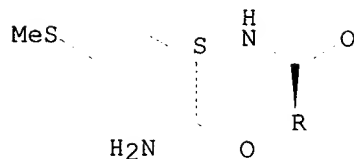
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125 ANSWER 44 OF 48 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:121773 CAPLUS
DOCUMENT NUMBER: 124:165817
TITLE: Calcitonin gene-related

Searched by Barb O'Bryen, STIC 308-4291

**peptide (8-37) does not antagonize
calcitonin gene-related
peptide in rat spinal cord**

AUTHOR(S):
CORPORATE SOURCE:

Xu, Xiao-Jun; Wiesenfeld-Hallin, Zsuzsanna
Department of Medical Laboratory Sciences and
Technology, Section of Clinical Neurophysiology,
Karolinska Institute, Huddinge University Hospital,
Huddinge, S-141 86, Swed.

SOURCE: Neuroscience Letters (1996), 204(3), 185-8
CODEN: NELED5; ISSN: 0304-3940

PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have examd. the effects of intrathecal (i.t.) human calcitonin gene-related peptide (hCGRP) and its C-terminal fragment hCGRP(8-37), a proposed CGRP antagonist, on the flexor reflex in decerebrate, spinalized, unanesthetized rats. The i.t. hCGRP at 26 pmol caused a moderate facilitation of the reflex which was not antagonized by hCGRP(8-37) at doses ranging from 26 pmol to 5.2 nmol. Furthermore, hCGRP(8-37) by itself facilitated the reflex, with no signs of inhibition. It is concluded that the spinal CGRP receptor mediating the spinal facilitatory effect of hCGRP is not antagonized by hCGRP(8-37). Thus, it is unlikely that hCGRP(8-37) can be useful as a spinal analgesic.

IT 119911-68-1

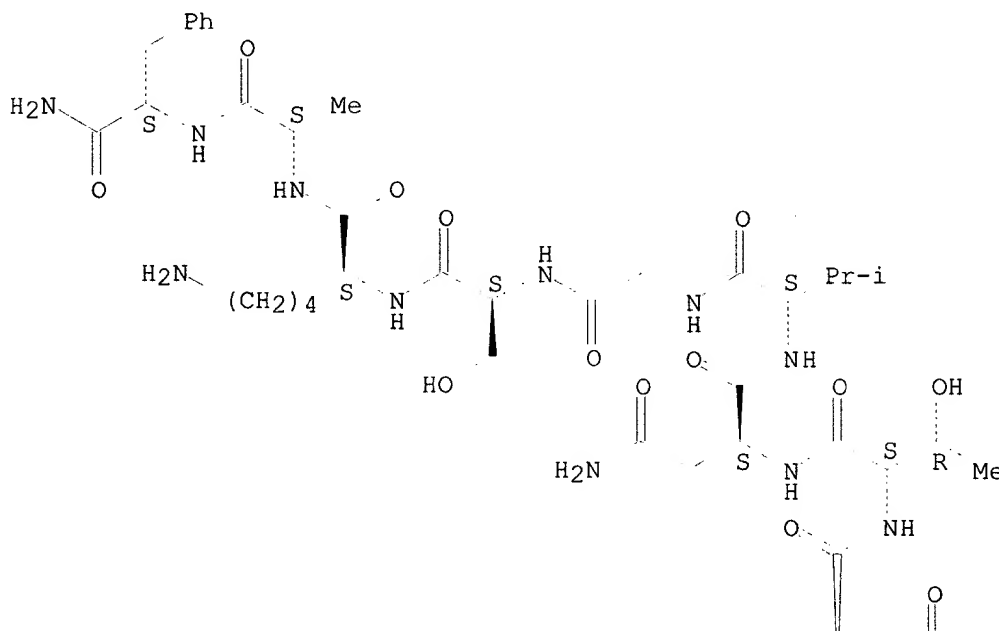
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CGRP fragment does not antagonize CGRP
in rat spinal cord)

RN 119911-68-1 CAPLUS

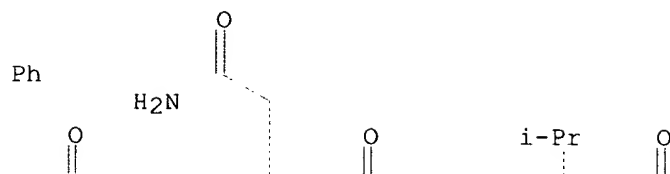
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

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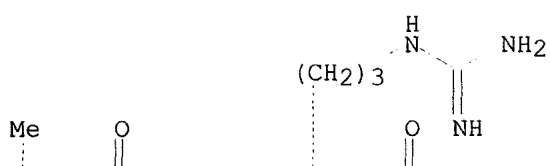
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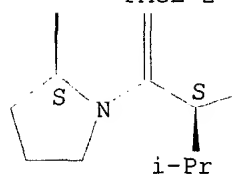
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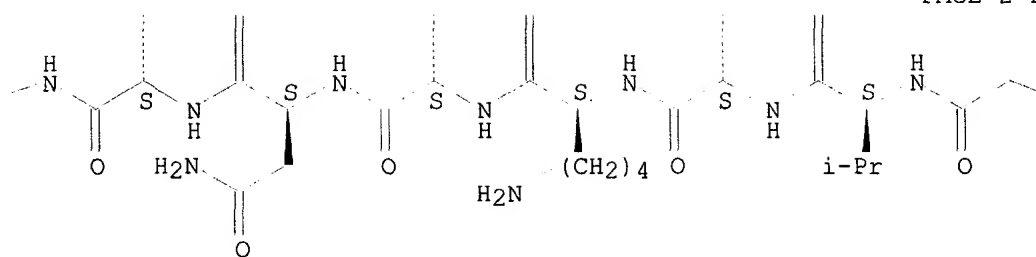
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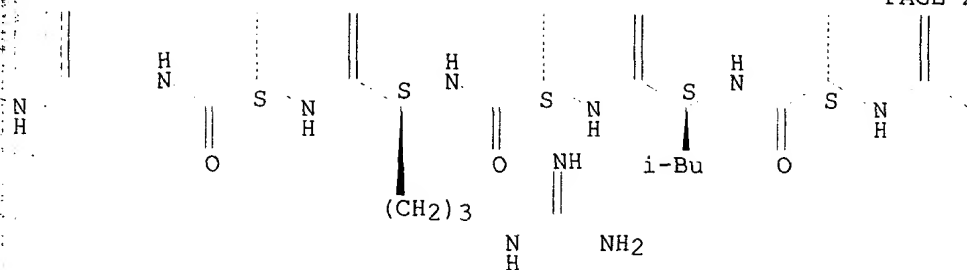
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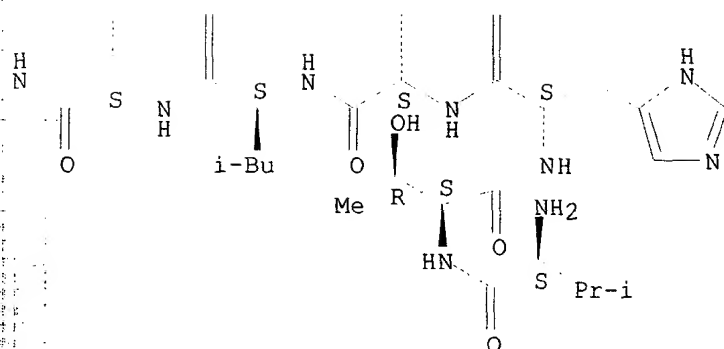
PAGE 2-B



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B25 ANSWER 45 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:94517 CAPLUS

DOCUMENT NUMBER: 124:136154

TITLE: Attenuation of the anorectic effects of glucagon, cholecystokinin, and bombesin by the amylin receptor antagonist CGRP (8-37)

AUTHOR(S): Lutz, T. A.; Del Prete, E.; Szabady, M. M.; Scharrer, E.

CORPORATE SOURCE: Inst. Veterinary Physiology, Univ. Zurich, Zurich, 8057, Switz.

SOURCE: Peptides (Tarrytown, New York) (1996), 17(1), 119-24
CODEN: PPTDD5; ISSN: 0196-9781

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The anorectic effect of i.p. injection of amylin (1 .mu.g/kg) was abolished by simultaneous i.p. injection of the amylin receptor antagonist CGRP(8-37) [CGRP(8-37), 10 .mu.g/kg]. The i.p. injection of pancreatic glucagon (400 .mu.g/kg) at dark onset also reduced food intake in 24-h food-deprived rats, and this effect was also totally blocked by coadministration of CGRP(8-37) (10 .mu.g/kg). In another feeding paradigm with glucagon (540 .mu.g/kg i.p. 3 h into the light phase in 3 h-prefed rats), however, the anorectic effect of glucagon was not significantly antagonized by CGRP(8-37). The anorectic effect of cholecystokinin (CCK) (0.25 .mu.g/kg) and bombesin (BBS) (2 .mu.g/kg) was partly neutralized by CGRP(8-37). In contrast, the anorectic effect of vasopressin (VP) (2.5 .mu.g/kg) was not influenced by CGRP(8-37). As glucagon has been shown previously to increase the secretion of amylin, the authors conclude that the anorectic effect of peripherally administered glucagon is mediated by

the release of amylin, at least under certain conditions. This may also be true for CCK and BBS, as these peptides are insulinotropic and may therefore be presumed to increase amylin release.

IT 31362-50-2, Bombesin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

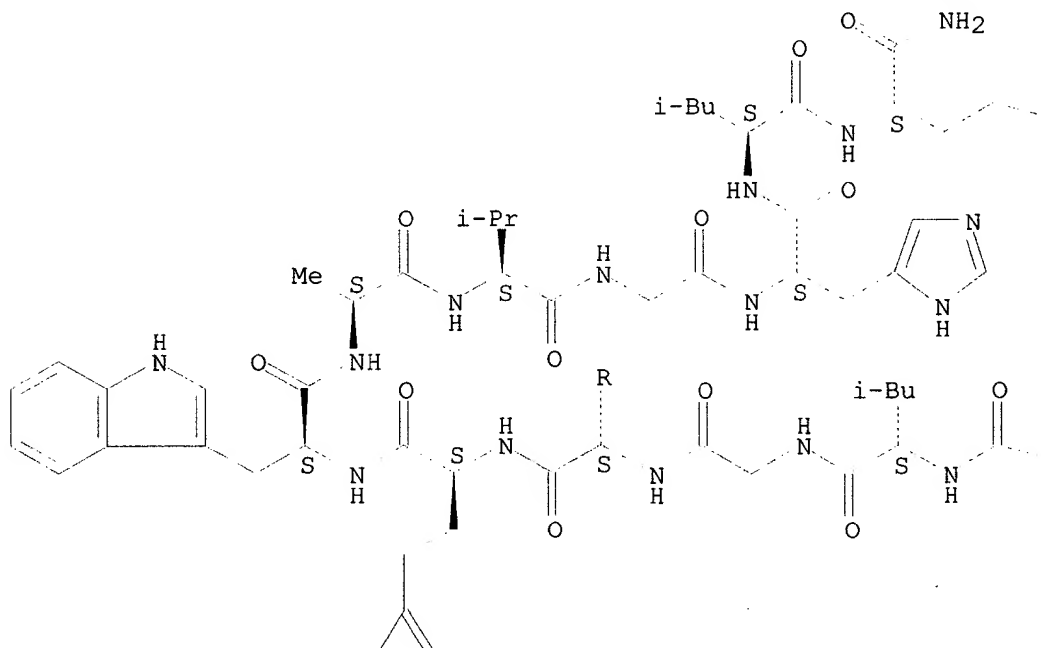
(attenuation of anorectic effects of glucagon, cholecystokinin, and bombesin by amylin receptor antagonist CGRP (8-37))

RN 31362-50-2 CAPLUS

CN Bombesin (9CI) (CA INDEX NAME)

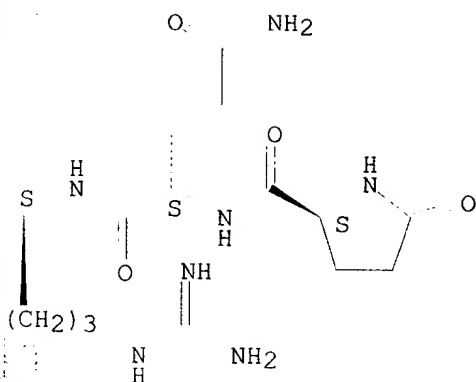
Absolute stereochemistry.

PAGE 1-A

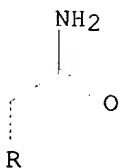
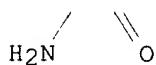


PAGE 1-B

SMe



PAGE 2-A



E25 ANSWER 46 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:785998 CAPLUS

DOCUMENT NUMBER: 123:189279

TITLE: Proadrenomedullin NH₂-terminal 20 peptide, a new product of the adrenomedullin gene, inhibits norepinephrine overflow from nerve endings

AUTHOR(S): Shimomura, Tatsuo; Ito, Yasushi; Ando, Katsuyuki; Kitamura, Kazuo; Kangawa, Kenji; Fujita, Toshiro

CORPORATE SOURCE: Fourth Dep. of Internal Medicine, Univ. of Tokyo Sch. of Medicine, Tokyo, 112, Japan

SOURCE: J. Clin. Invest. (1995), 96(3), 1672-6

CODEN: JCINAO; ISSN: 0021-9738

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Proadrenomedullin NH₂-terminal 20 peptide (PAMP) and adrenomedullin, which are derived from proadrenomedullin, exhibit remarkable hypotensive action. The effect of PAMP and adrenomedullin on peripheral sympathetic neural transmission was studied. Using perfused rat mesenteric arteries, PAMP (0, 1, 5, and 10 pmol/mL) decreased norepinephrine overflow by

periarterial elec. nerve stimulation in a dose-dependent fashion (0.244 \pm 0.043, 0.231 \pm 0.048, 0.195 \pm 0.061, and 0.168 \pm 0.051 ng/g tissue wt.: NS, $P < 0.05$, and $P < 0.02$, resp.). In contrast to PAMP, adrenomedullin (1, 5, and 10 pmol/mL) did not change it. In contrast, vasoconstrictive response of mesenteric arteries to exogenous norepinephrine was significantly attenuated by 10 pmol/mL of adrenomedullin but not by the same dose of PAMP. Calcitonin gene-related peptide (8-37) [CGRP(8-37)], a CGRP receptor antagonist, inhibited the vasodilatory effect of adrenomedullin but could not suppress the sympathoinhibitory effect of PAMP. Neither a nicotinic antagonist, hexamethonium, nor a presynaptic α_2 antagonist, yohimbine, blocked the sympathoinhibitory effect of PAMP. Thus, it suggests that PAMP and adrenomedullin, which are derived from the same gene, exhibit different hypotensive mechanisms: PAMP inhibits neural transmission at peripheral sympathetic nerve ending, although adrenomedullin directly dilates vascular smooth muscle, possibly through CGRP-like receptor.

IT 167699-60-7

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

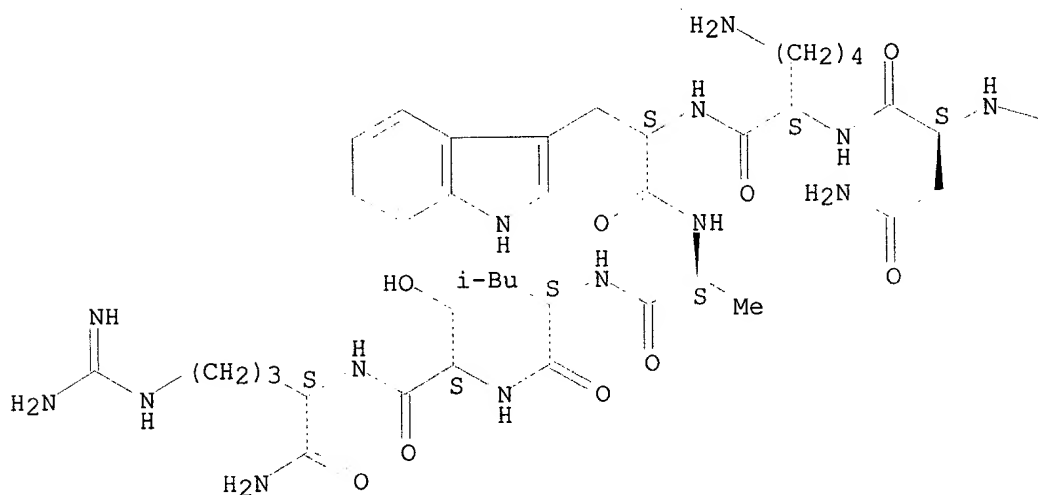
(proadrenomedullin NH2-terminal 20 peptide inhibition of norepinephrine overflow from nerve endings)

RN 167699-60-7 CAPLUS

CN L-Argininamide, L-alanyl-L-arginyl-L-leucyl-L-.alpha.-aspartyl-L-threonyl-L-seryl-L-seryl-L-glutamyl-L-phenylalanyl-L-arginyl-L-lysyl-L-lysyl-L-tryptophyl-L-asparaginyl-L-lysyl-L-tryptophyl-L-alanyl-L-leucyl-L-seryl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



Chemical structure of the polymer repeat unit is shown below:

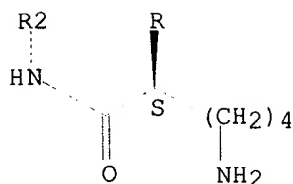
$$\begin{array}{c} \text{O} \\ | \\ \text{HN} \text{---} \text{S} \text{---} (\text{CH}_2)_4 \text{---} \text{NH}_2 \\ | \\ \text{S} \end{array}$$

The structure is a linear polymer chain with a repeating unit of $[\text{HN}(\text{O})\text{S}(\text{CH}_2)_4\text{NH}_2]$. The HN group is connected to an O atom, which is connected to an S atom. The S atom is connected to a $(\text{CH}_2)_4$ chain, which is connected to an NH_2 group. The NH_2 group is connected to another S atom, which is connected to another HN group, completing the repeat unit.

Chemical structure of a cyclic peptide derivative, showing a 12-membered ring with various substituents and stereochemistry. The structure includes a side chain with a $(CH_2)_3$ group, a phenyl (Ph) group, a methyl (Me) group, a carboxylic acid (CO_2H) group, and a butyl ($Bu-i$) group. Stereochemistry is indicated with wedges and dashes.

CCSCCNC(=O)NCCCNC(=O)N

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L25 ANSWER 47 OF 48 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:622562 CAPLUS

DOCUMENT NUMBER: 121:222562

TITLE: **Inhibitory effect of calcitonin-gene related peptide on substance P-induced superoxide production by neutrophils**

AUTHOR(S): Tonabe, Takatoshi; Otani, Hitomi; Ninomiya, Toshinori; Ogawa, Ryoukei; Inagaki, Chiyoko

CORPORATE SOURCE: Department Pharmacology and Orthopedic Surgery, Kansai Medical University, Osaka, 570, Japan

SOURCE: Ensho (1994), 14(3), 207-12
CODEN: ENSHEE; ISSN: 0389-4290

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB Calcitonin gene-related peptide (CGRP) is known to be co-localized with substance P (SP) in sensory C-fibers. The authors investigated the interaction between these neuropeptides in the superoxide (O₂) prodn. of human neutrophils. SP and SP4-11 fragment (10.apprx.100 .mu.M) induced O₂ prodn. of neutrophils in a dose-dependent manner. Phospholipase C inhibitor, U-73122 and neomycin, suppressed the O₂ prodn. by SP and SP4-11 fragment. CGRP (10.apprx.20 .mu.M) reduced the SP-induced O₂ prodn., and this effect of CGRP was blocked by CGRP receptor antagonist, CGRP8-37 (10 .mu.M). Dibutyrylcyclic AMP (dBcAMP; 0.5 mM) and phosphodiesterase inhibitors, 3-isobutyl-1-Me xanthine (IBMX, 5 .mu.M) and theophylline (0.5 mM), also inhibited SP-induced O₂ prodn. The cAMP-dependent protein kinase (A-kinase) inhibitors, H-8 (10 .mu.M) and KT5720 (50 nM), suppressed the CGRP-induced effect. These data suggest that CGRP inhibits the SP-induced O₂ prodn. in neutrophils by interfering with phosphoinositide signaling through receptor-linked activation of the cAMP/A-kinase-dependent pathway.

IT 33507-63-0, Substance P (peptide)

RL: BAC (Biological activity or effector, except adverse); BIOL
(Biological study)

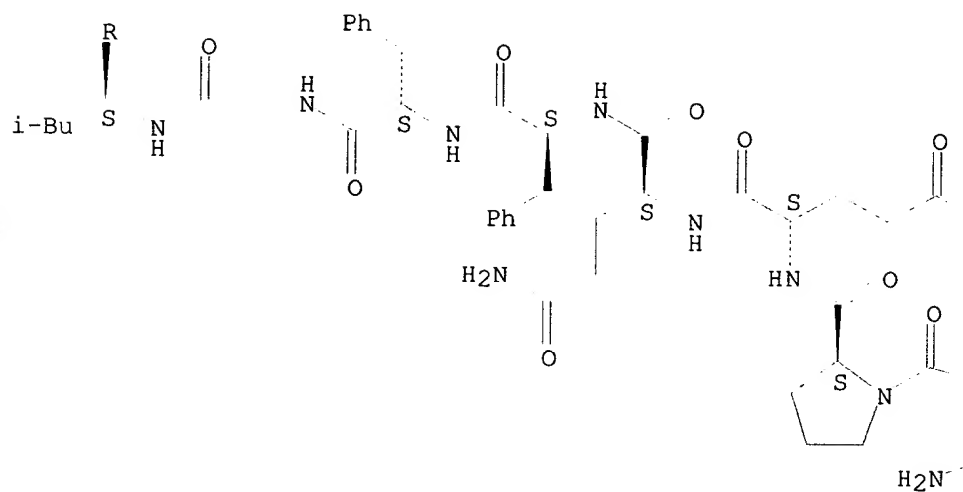
(inhibitory effect of calcitonin-gene
related peptide on substance P-induced superoxide
prodn. by neutrophils)

RN 33507-63-0 CAPLUS

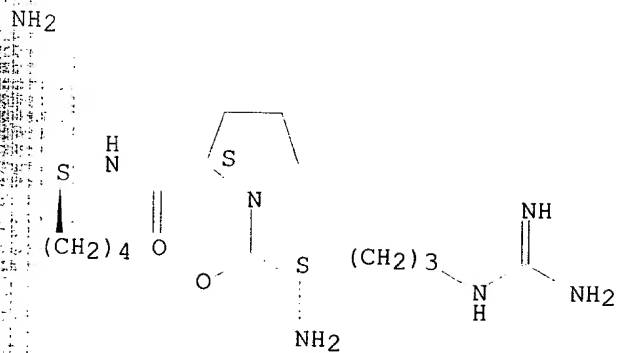
CN Substance P (9CI) (CA INDEX NAME)

Absolute stereochemistry.

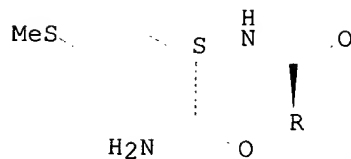
PAGE 1-A



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L25 ANSWER 48 OF 48

ACCESSION NUMBER:

DOCUMENT NUMBER:

TITLE:

CAPLUS COPYRIGHT 2002 ACS

1992:420667 CAPLUS

117:20667

Structure-activity study of hCGRP8-37, a

Searched by Barb O'Bryen, STIC 308-4291

**calcitonin gene-related
peptide receptor antagonist**

AUTHOR(S): Mimeault, Murielle; Quirion, Remi; Dumont, Yvan;

CORPORATE SOURCE: St-Pierre, Serge; Fournier, Alain

Inst. Natl. Rech. Sci.-Sante, Univ. Quebec,
Pointe-Claire, PQ, H9R 1G6, Can.

SOURCE: J. Med. Chem. (1992), 35(12), 2163-8

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A structure-activity study was carried out to det. the importance of the N-terminal amino acids of human calcitonin gene-related peptide (8-37) (hCGRP8-37) in binding and antagonistic activity to CGRP receptors. Therefore, fragments of hCGRP8-37 as well as analogs obtained by the replacement of residues 9-12 by L-alanine were synthesized by solid phase peptide synthesis, using BOP as a coupling reagent. The affinities of the peptides to CGRP receptors were evaluated in the rat brain, guinea pig atrium, and guinea pig vas deferens membrane preps. Their antagonistic activities were measured in the guinea pig atria and rat vas deferens bioassays. The pharmacol. characterization showed that arginine-11 and leucine-12 play a crucial role for the affinity of hCGRP8-37. Interestingly, [Ala11]hCGRP8-37 was able to potentiate the twitch response of the elec. stimulated rat vas deferens. On the other hand, the substantial antagonistic potencies of analogs [Ala9]-, [Ala10]-, and [Ala12]hCGRP8-37, as compared to those of the fragments hCGRP10-37, hCGRP11-37, and hCGRP12-37, suggest that the side-chains of Thr-9, His-10, and Leu-12 assume mainly a structural role. Accordingly, the conformational characterization of these peptides by CD spectroscopy revealed that the residues 9-12 are important for the integrity of the amphiphilic .alpha.-helix of hCGRP8-37.

IT 119911-68-1, Human **calcitonin gene-related peptide** (8-37) 119911-68-1D, Human **calcitonin gene-related peptide** (8-37), analogs and fragments 137339-75-4D, analogs and fragments 137339-76-5 137339-77-6 141017-70-1 141017-71-2 141017-72-3 141017-73-4

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

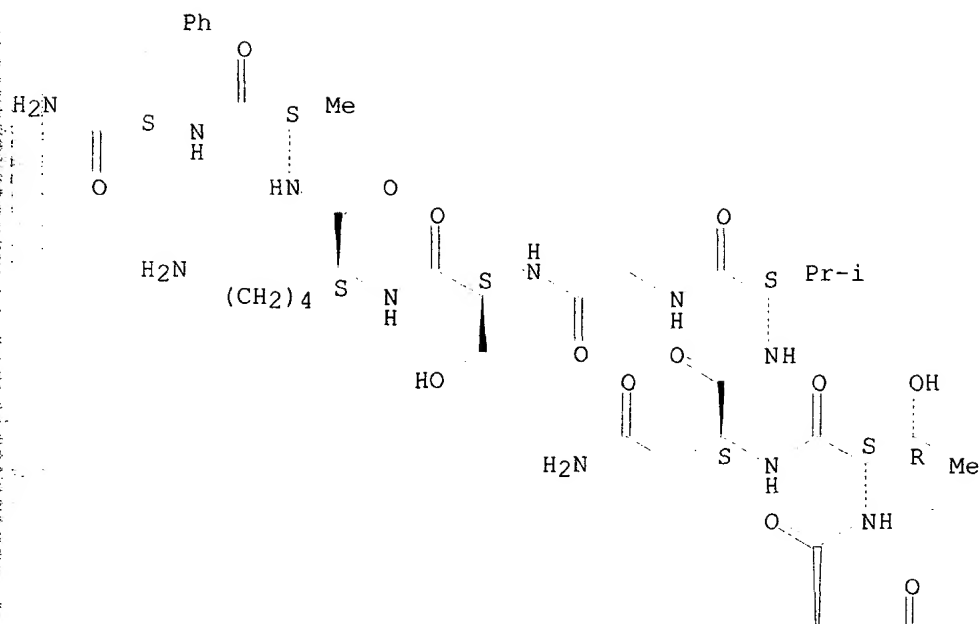
(**calcitonin gene-related peptide antagonist** activity of, in brain and heart atrium and vas deferens)

RN 119911-68-1 CAPLUS

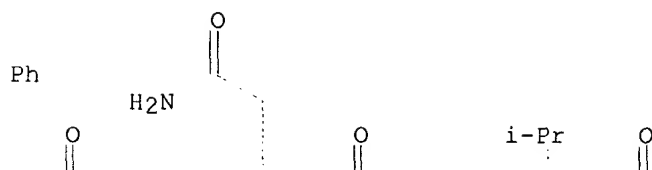
CN 8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



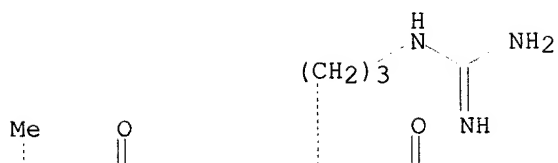
PAGE 1-B



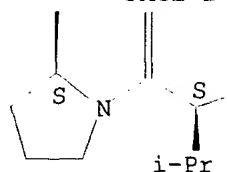
PAGE 1-C



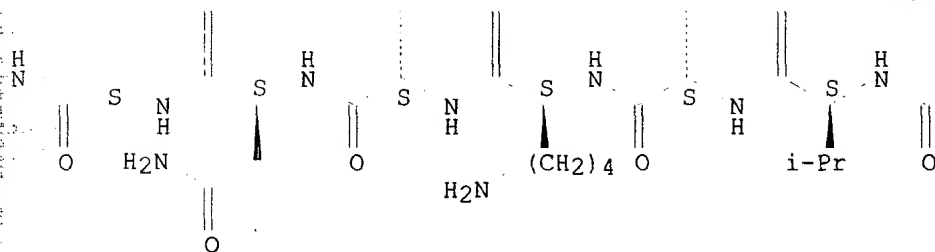
PAGE 1-D



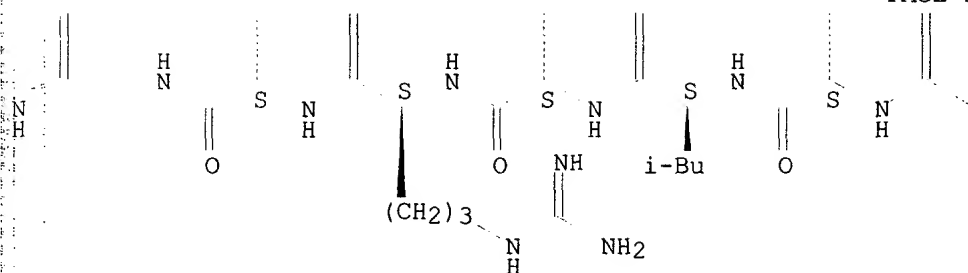
PAGE 2-A



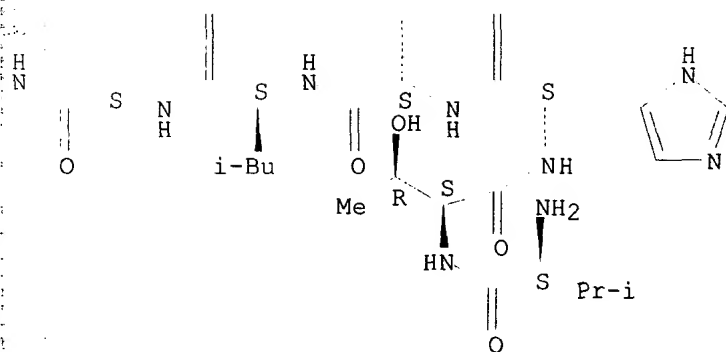
PAGE 2-B



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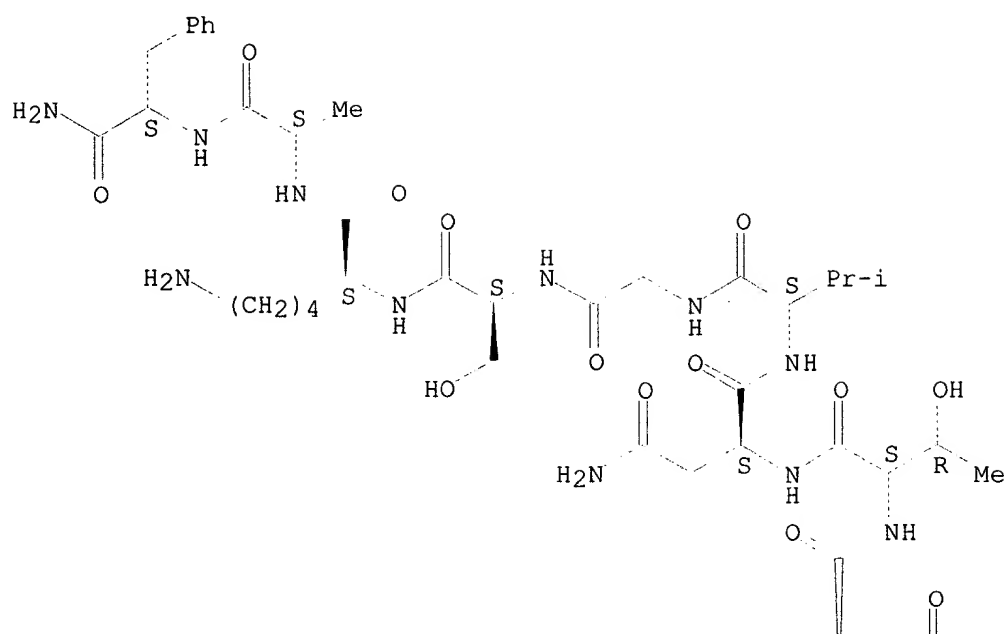


119911-68-1 CAPLUS

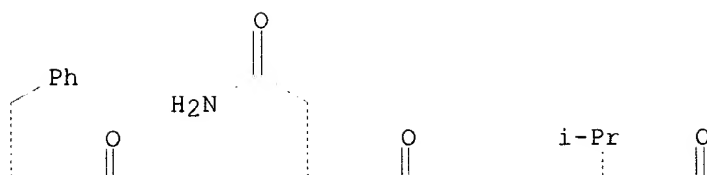
8-37-.alpha.-Calcitonin gene-related peptide (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



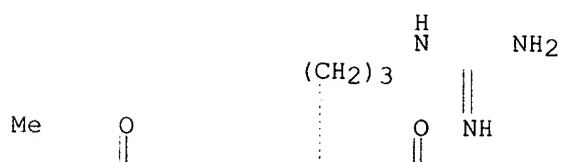
PAGE 1-B



PAGE 1-C



PAGE 1-D

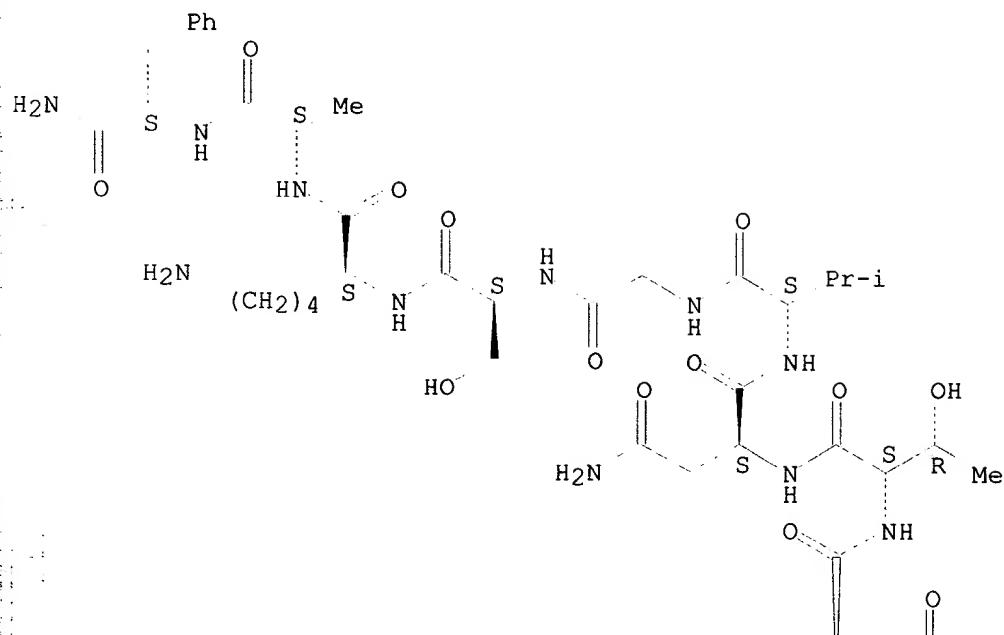


The image shows three chemical structures of thiazine derivatives. The first structure on the left is 2,4,6-triamino-1,3,5-triazine-2,4,6-trisulfonamide, which is a triazine ring with amino groups at positions 2, 4, and 6, and sulfonamide groups at positions 1, 3, and 5. The middle structure is 2,4,6-triamino-1,3,5-triazine-2,4,6-trisulfonamide, which is a triazine ring with amino groups at positions 2, 4, and 6, and sulfonamide groups at positions 1, 3, and 5. The third structure on the right is 2,4,6-triamino-1,3,5-triazine-2,4,6-trisulfonamide, which is a triazine ring with amino groups at positions 2, 4, and 6, and sulfonamide groups at positions 1, 3, and 5.

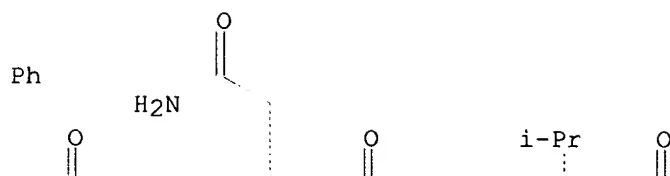
RN	137339-75-4	CAPLUS
CN	.alpha.-Calcitonin gene-related peptide (human reduced), 1-de-L-alanine-2-de-L-cysteine-3-de-L-aspartic acid-4-de-L-threonine-5-de- L-alanine-6-de-L-threonine-7-de-L-cysteine-8-de-L-valine- (9CI) (CA INDEX NAME)	

Absolute stereochemistry.

PAGE 1-A



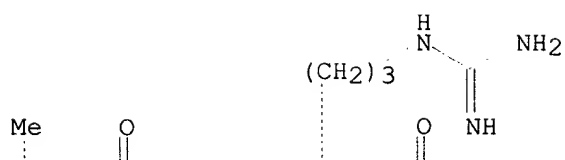
PAGE 1-B



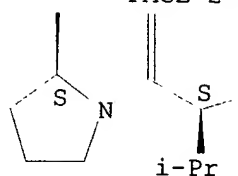
PAGE 1-C



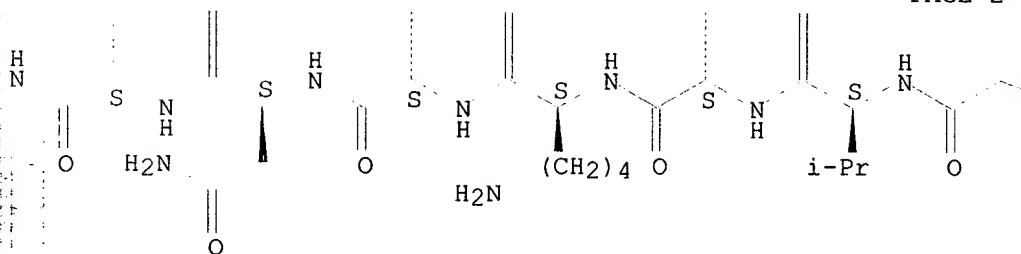
PAGE 1-D



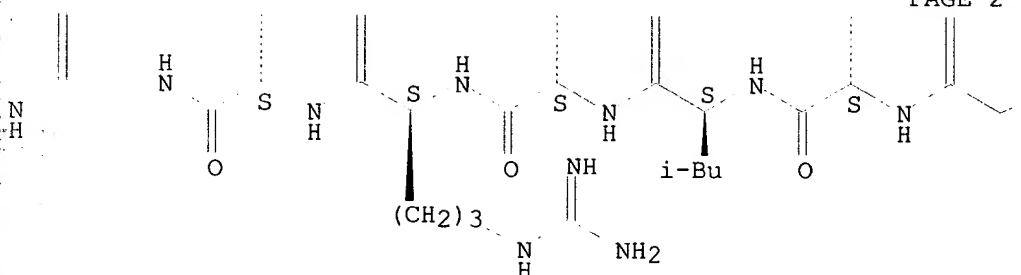
PAGE 2-A



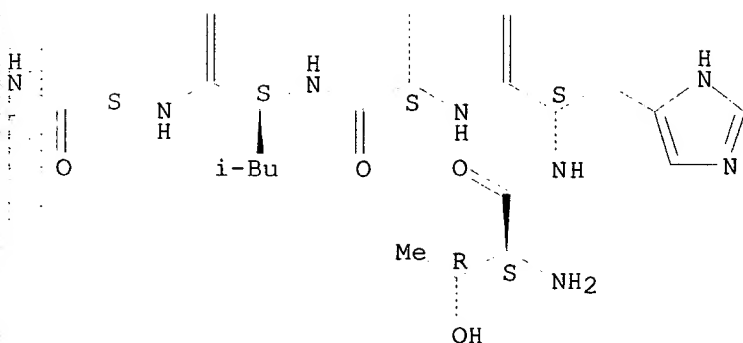
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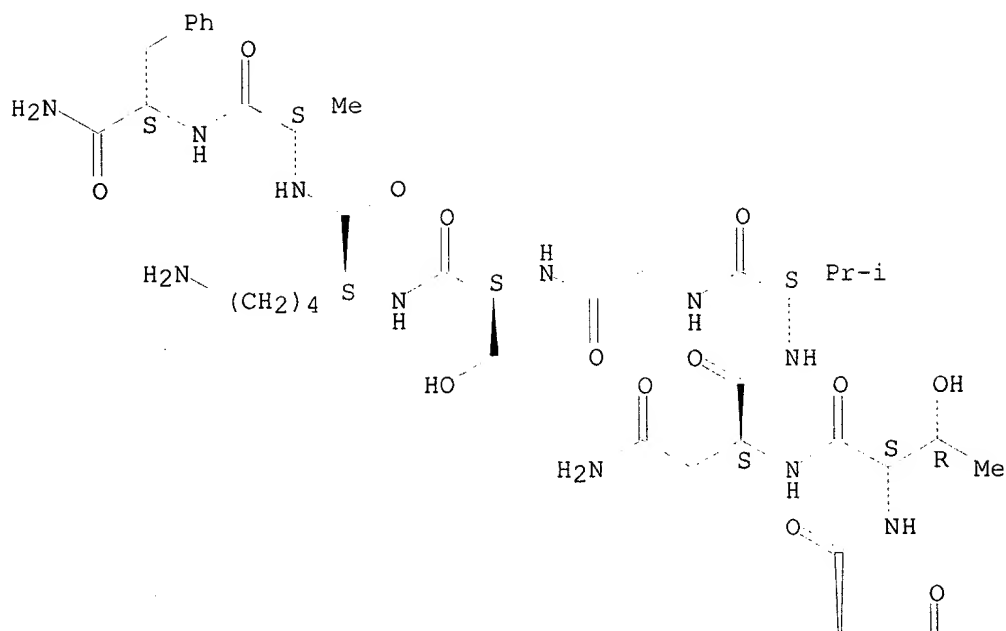


137339-76-5 CAPLUS

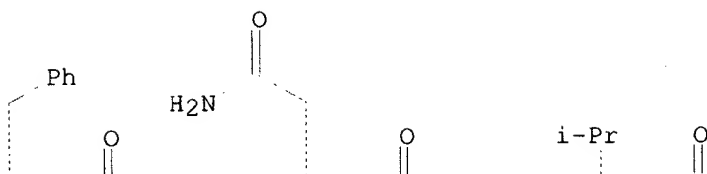
.alpha.-Calcitonin gene-related peptide (human reduced),
 1-de-L-alanine-2-de-L-cysteine-3-de-L-aspartic acid-4-de-L-threonine-5-de-
 L-alanine-6-de-L-threonine-7-de-L-cysteine-8-de-L-valine-9-de-L-threonine-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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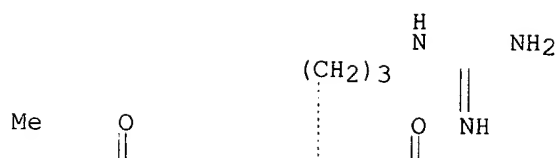
PAGE 1-B



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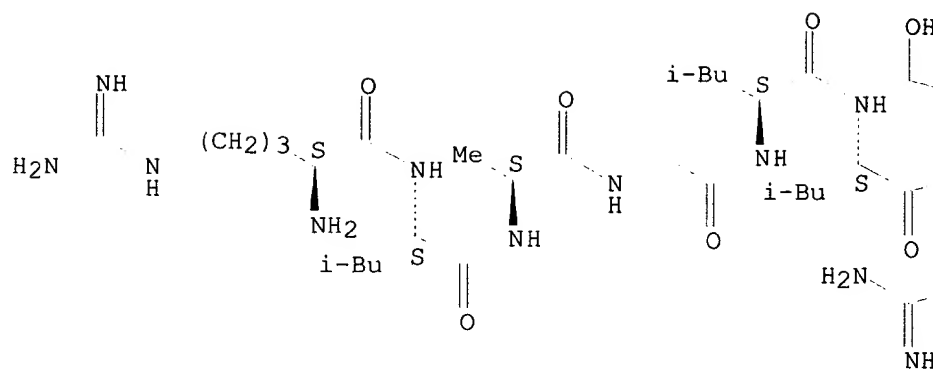
The image shows two chemical structures. The left structure is 2,3-dihydro-1,4-dithiane, a six-membered ring with two sulfur atoms (S) and two nitrogen atoms (N). The right structure is 2,3-dihydro-1,4-dithiane with an isopropyl group (i-Pr) attached to one of the sulfur atoms.

The image displays three chemical structures of 1,3,5-thiazine derivatives, labeled 1, 2, and 3. Each structure consists of a central six-membered ring with a nitrogen atom at position 1 and a sulfur atom at position 3. The ring is substituted at positions 2, 4, and 6. In structure 1, the substituents are an amide group (-NH-C(=O)-), a thioamide group (-NH-C(=S)-), and a thioether group (-S-CH₂-). In structure 2, the substituents are a thioether group (-S-CH₂-), a thioamide group (-NH-C(=S)-), and a thioether group (-S-CH₂-). In structure 3, the substituents are a thioether group (-S-CH₂-), a thioamide group (-NH-C(=S)-), and a thioether group (-S-CH₂-).

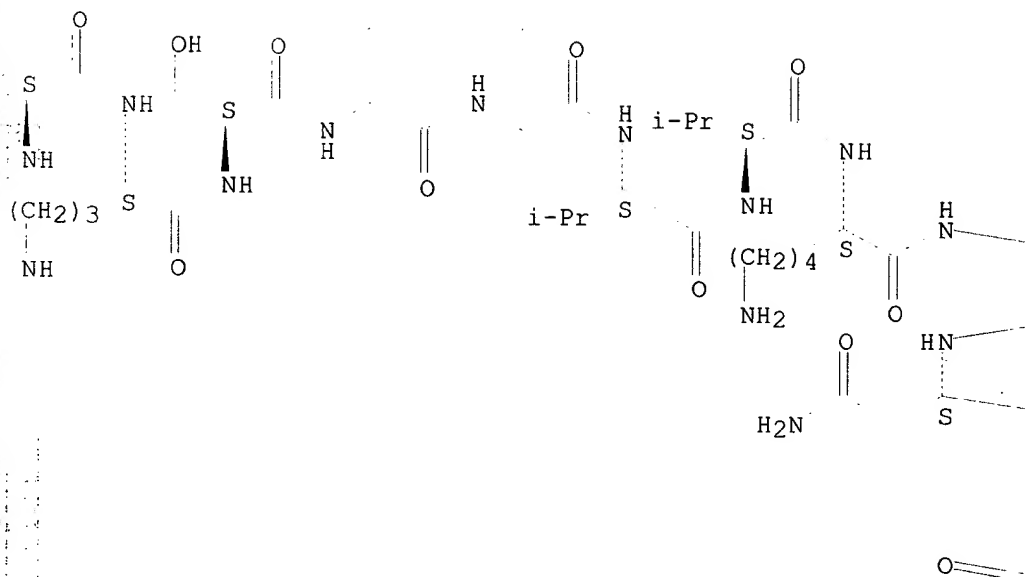
NC(=O)N[C@@H](CCCCNC(=O)N)C(=O)N[C@@H](CCCCNC(=O)N)C(=O)N[C@@H](CCCCNC(=O)N)C(=O)N

Absolute stereochemistry.

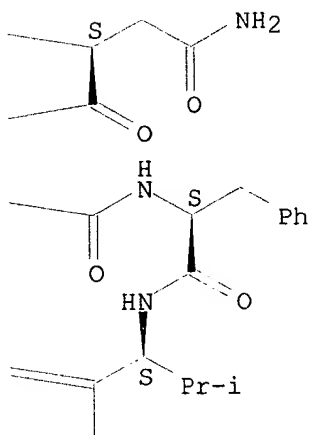
PAGE 1-A



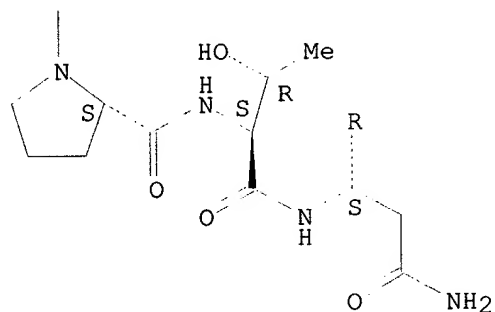
PAGE 1-B



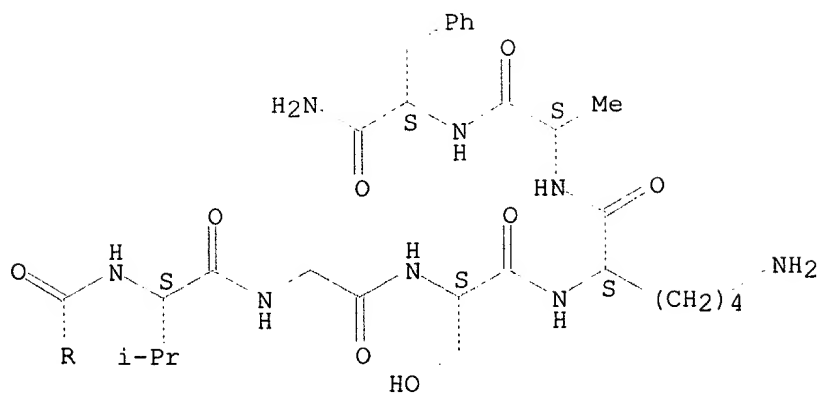
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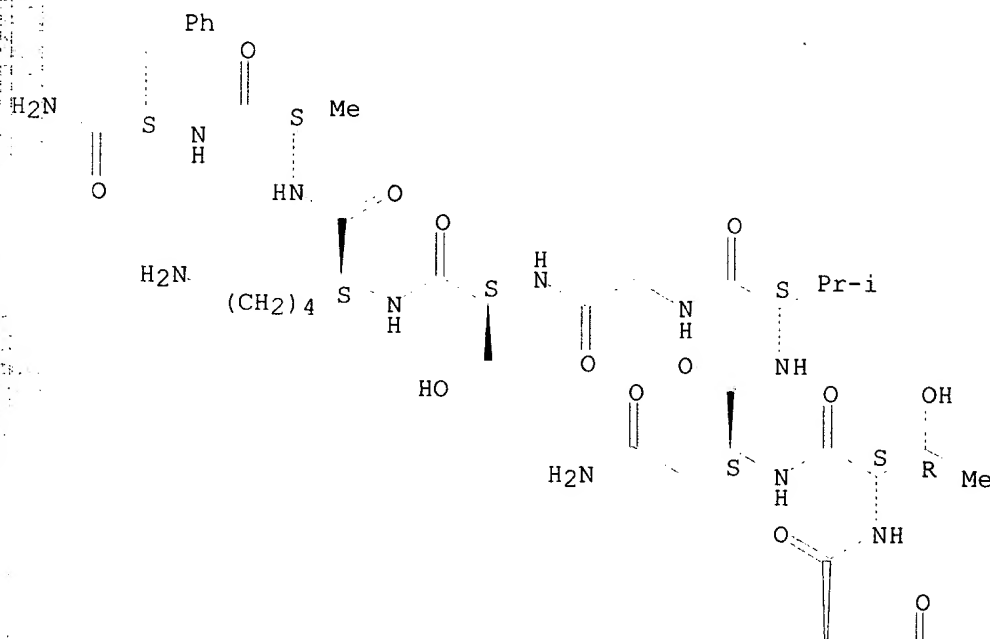
PAGE 3-A



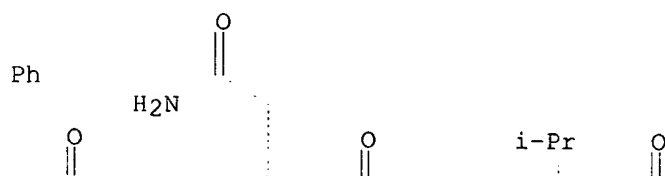
RN 141017-70-1 CAPLUS
CN .alpha.-Calcitonin gene-related peptide (human reduced),
1-de-L-alanine-2-de-L-cysteine-3-de-L-aspartic acid-4-de-L-threonine-5-de-
L-alanine-6-de-L-threonine-7-de-L-cysteine-9-L-alanine- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

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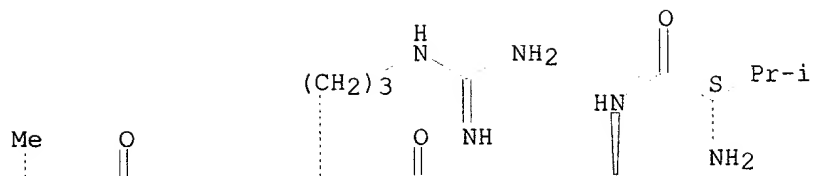
PAGE 1-B



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C[C@H](N1CCCC1)C(=O)N(C)C

PAGE 2

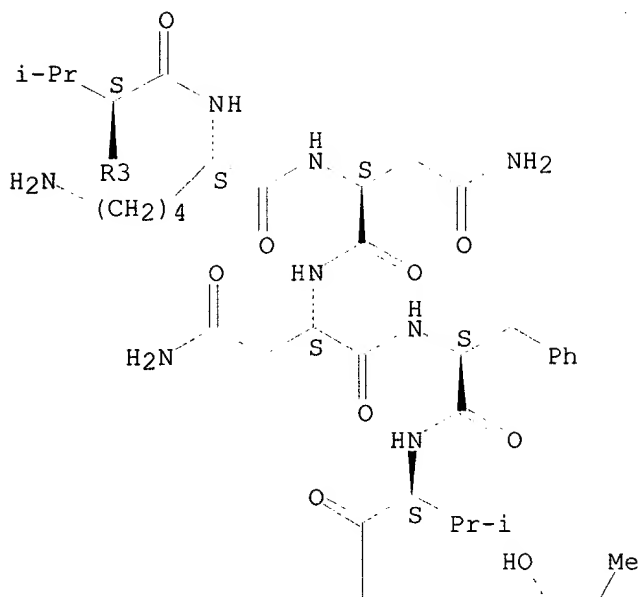
Chemical structure of the repeating unit of poly(2,2'-(1,3-phenylene)-5,5'-bis(4-aminobenzothioether)) is shown below:

The structure is a repeating unit of a polymer, indicated by the subscript n in brackets. It features a central 1,3-phenylene ring (a benzene ring with substituents at the 1 and 3 positions). This central ring is connected at its 2 and 2' positions to two 4-aminobenzothioether groups. Each 4-aminobenzothioether group consists of a benzene ring with an amino group (NH_2) at the 4-position and a thioether linkage (S) at the 1-position. The thioether linkages connect to the 2 and 2' positions of the central phenylene ring. The repeating unit is enclosed in brackets with a subscript n .

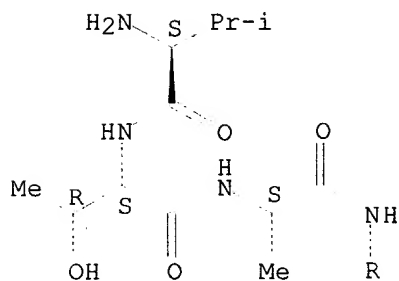
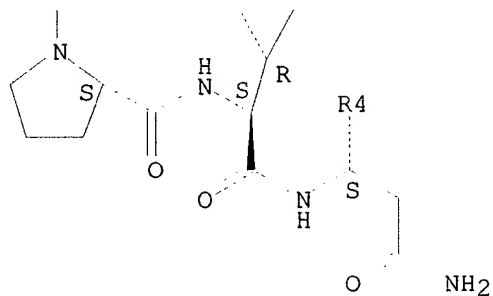
Chemical structures of 1,2,3,4-tetrahydro-6-methyl-5H-thiazolo[5,4-b]pyridine (1) and 1,2,3,4-tetrahydro-6-methyl-5H-thiazolo[5,4-b]pyridine-2-thione (2) are shown. Structure 1 is a bicyclic compound with a thiazole ring fused to a pyridine ring, with a methyl group at the 6-position. Structure 2 is the 2-thione derivative of 1, where the nitrogen at position 2 is replaced by a sulfur atom.

Absolute stereochemistry.

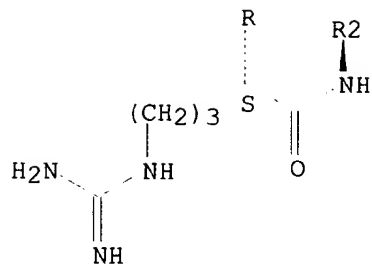
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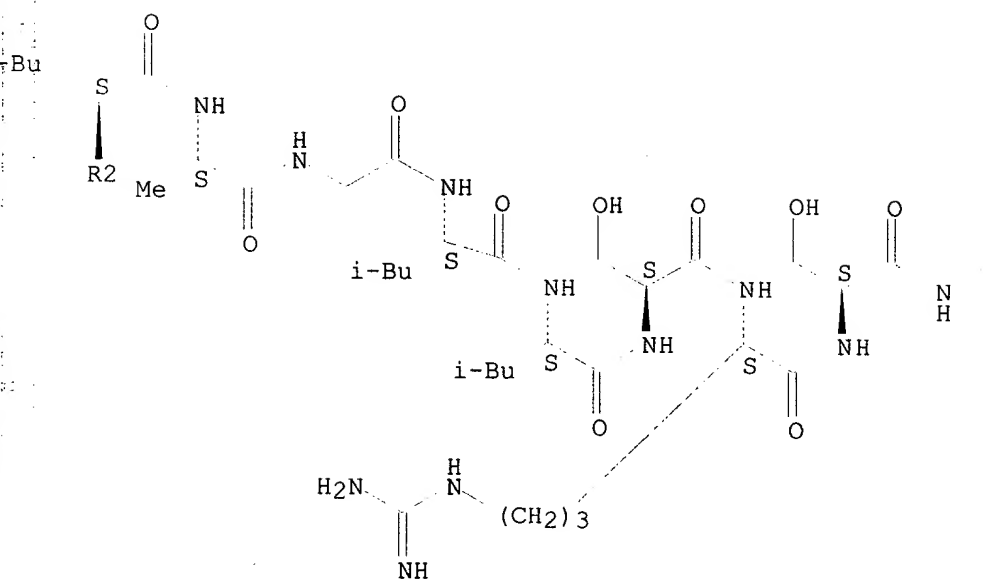
PAGE 2-A



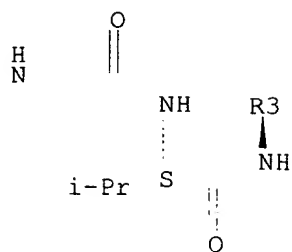
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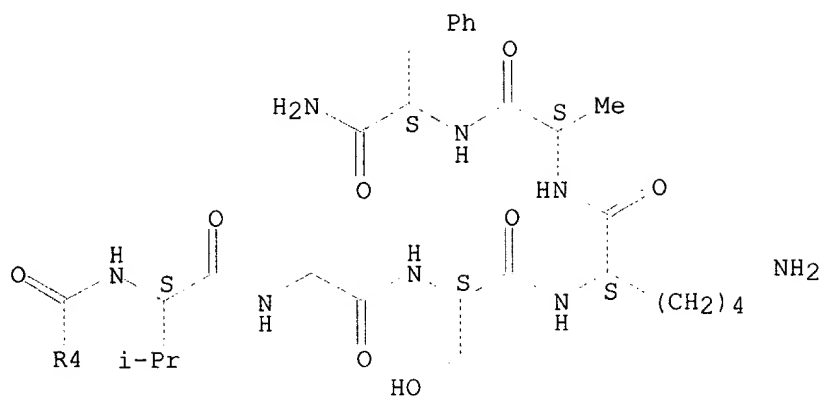
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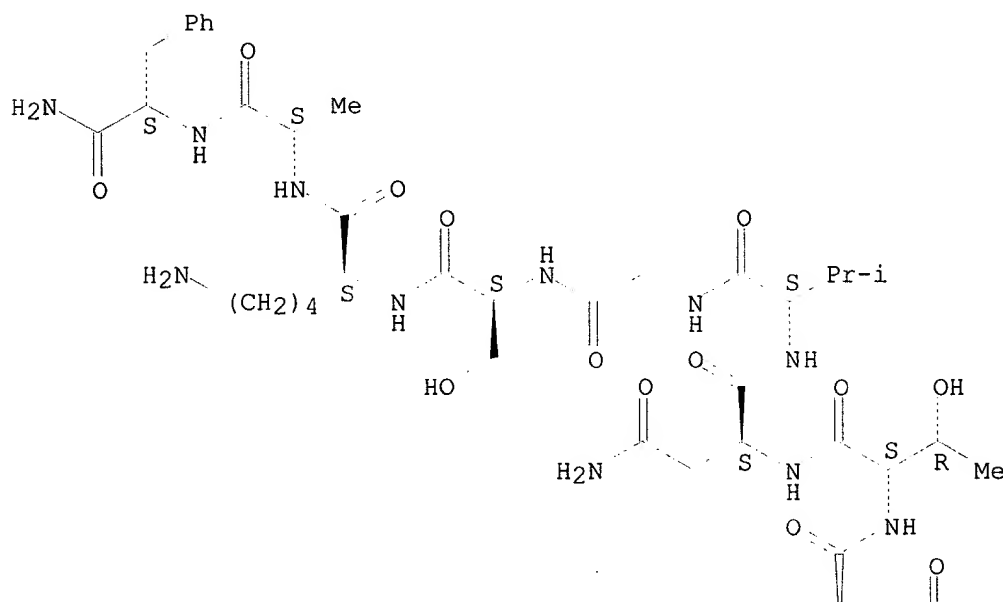


RN 141017-72-3 CAPLUS

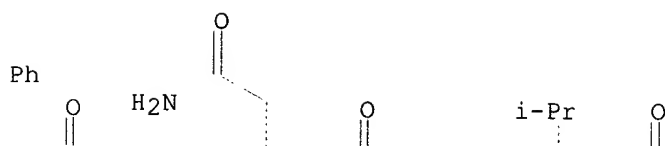
CN .alpha.-Calcitonin gene-related peptide (human reduced),
 1-de-L-alanine-2-de-L-cysteine-3-de-L-aspartic acid-4-de-L-threonine-5-de-
 L-alanine-6-de-L-threonine-7-de-L-cysteine-11-L-alanine- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

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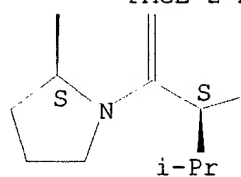
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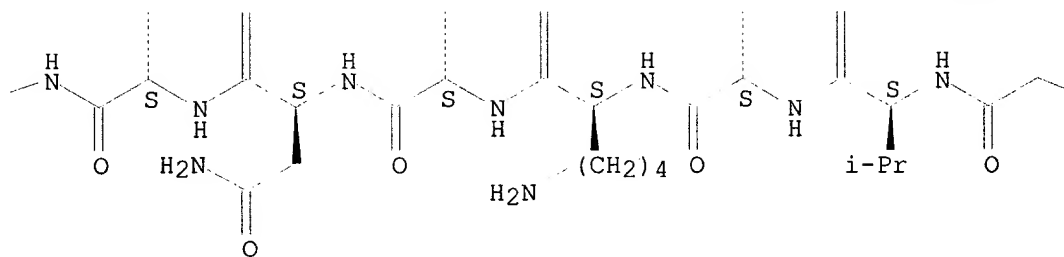
PAGE 1-D

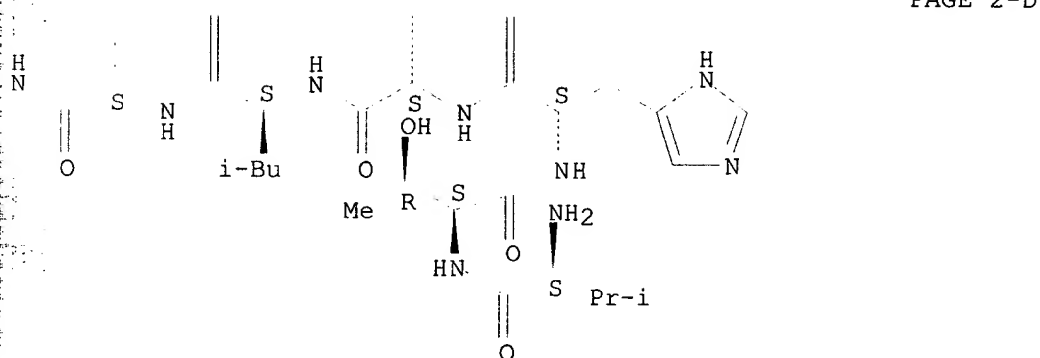
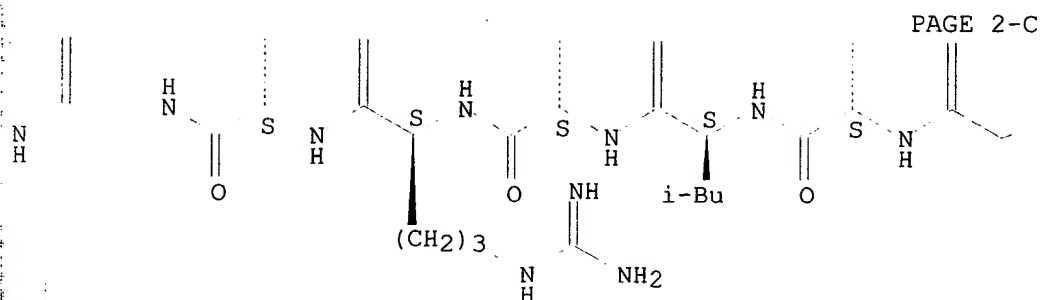


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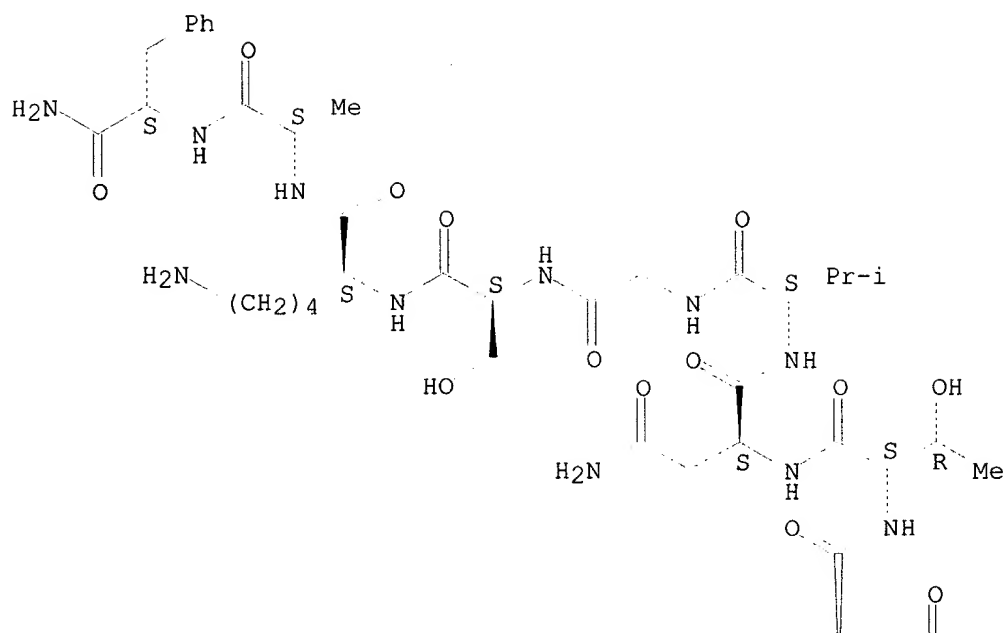




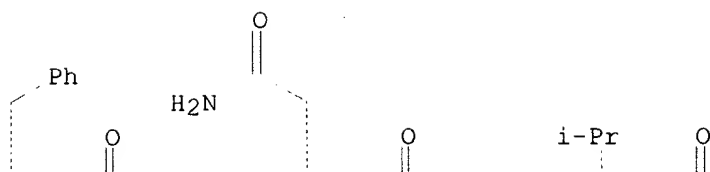
RN 141017-73-4 CAPLUS
 CN .alpha.-Calcitonin gene-related peptide (human reduced),
 1-de-L-alanine-2-de-L-cysteine-3-de-L-aspartic acid-4-de-L-threonine-5-de-
 L-alanine-6-de-L-threonine-7-de-L-cysteine-12-L-alanine- (9CI) (CA INDEX
 NAME)

Absolute stereochemistry.

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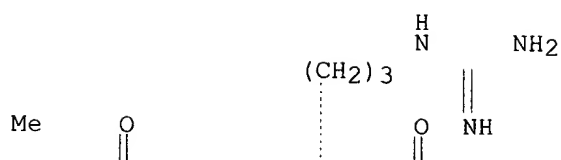
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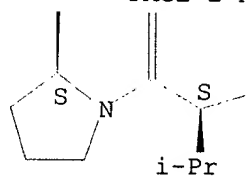
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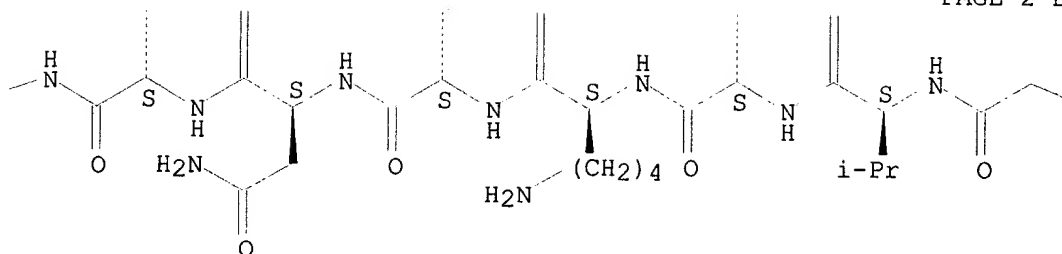
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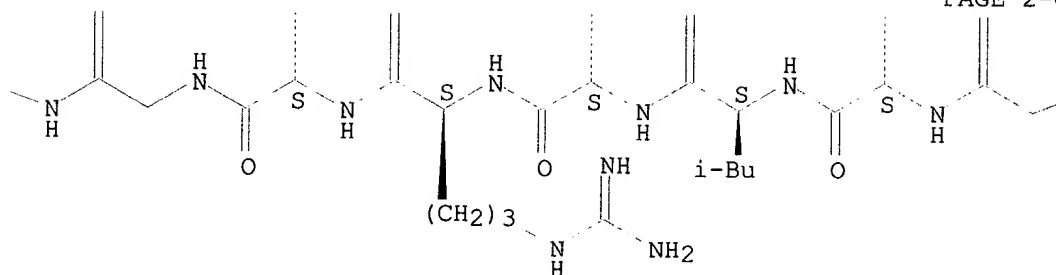
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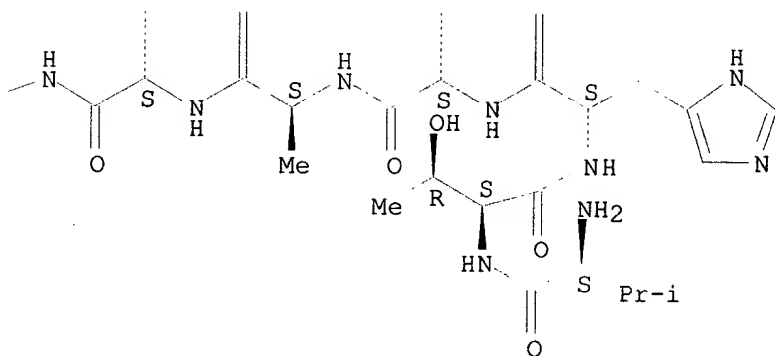
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Searched by Barb O'Bryen, STIC 308-4291

